

The
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Medicine and Surgery*

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Volume VII

Skin and Venereal Diseases

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SKIN AND VENEREAL DISEASES.

DERMATOSES.

RESEARCHES IN DERMATOLOGY.

The Etiology of Common Warts. The clinical evidence in favor of an infectious agent in the causation of warts is extremely suggestive. The appearance of so-called daughter warts following the initial appearance of a large wart, the appearance of warts on contiguous and apposing surfaces, so frequently observed, the occasional occurrence in small groups of individual warts in close association, all lend color to this view. Wile and Kingery¹ report some interesting results of their experimental work on the etiology of these common and very troublesome lesions. Within the last few years, similar studies have been made by Ormsby and others in connection with verrucae plantaris.

The authors undertook to produce localized hyperkeratoses by the injection of a filtrate of wart material, because it was their belief that warts might possibly be caused by a filtrable virus.

The wart material was taken by curettement and divided into two portions. One portion was placed in glycerine for a later experiment. The remaining half was immediately ground up in a mortar with an exceedingly small amount of physiologic sodium chloride solution. This mash was then passed through a small Berkefeld filter, the filtering surface of which had been reduced by sealing all but the upper surface with paraffin. The resultant filtrate, gathered under negative pressure, was immediately placed on slant agar to test its sterility, which was uniformly negative. It was then injected by

(1) Jour. Amer. Med. Ass'n., Sept. 27, 1919.

means of a fine needle on a tuberculin syringe intracutaneously into the skin of the hands of themselves and assistants.

The experimental work demonstrates conclusively, the authors think, that the sterile filtrate of wart material injected intracutaneously is capable of producing localized hyperkeratoses which are clinically and pathologically identical with *verrucae vulgaris*. The initial experimental lesion starts as a flat wart which in no way differs from that seen in *verruca plana*. Interpapillary hypertrophy, inflammation and marked hyperkeratosis occur as secondary traumatic manifestations, whereas the initial change consists of an acanthosis and flattening of the papillae. Without denying that it is still possible that localized hyperkeratosis resembling *verrucae* may be due to traumas or foreign bodies, it is definitely demonstrated that such changes can be caused by a filtrable virus. It is not unlikely that when trauma and foreign bodies apparently are present as inciting factors they may merely represent the point of entrance of an infectious agent such as has been determined in these experiments (Plate I).

[In a personal communication recently received from Dr. Wile he reports that he has been able to produce warts in the second generation. That is to say, the second transplants of experimental warts have given positive results. He is convinced that all warts begin as flat papules, such as are seen in *verruca planae*, and that the secondary hypertrophy is the result of time and irritation only.—M.]

Inoculability of *Verruca Accuminata*. The etiology of the venereal wart has long been a subject for speculation and experimentation. A number of authors (Juliusberg, Dreyer, Notthaft, Heidingsfeld) hold this lesion to be due to a definite organism and have referred to the lesion as the "fourth venereal disease." Other authors (Geny, Diday, Rasch) believe in the identity of the venereal and the hard warts. The work of Walsch tends to substantiate the latter view. Other workers (Brumm, Taylor, Petters, Cronquist) look upon the pointed wart as a product of local irritation and infection. An old conception of the disorder is that it is due directly to

gonorrhea, but cases are not infrequently seen in which there is no evidence of gonorrhea.

The results of the experimental work of Tièche² are not in accord with those of Dolsch. Tièche was unable to produce experimentally the lesions on skin of the thigh, forearm or prepuce of patients who had verruca accuminata. Various preparations were made by grinding up the warts in salt solution and in distilled water. Only in one case was there a positive result and that occurred in an Italian laborer whose sexual abstinence could not be relied on.

In an attempt to effect a cure of verruca accuminata, a mixture of various lesions was made and autolyzed at from 60° to 80°. Subcutaneous injections of these autolysates caused sharp local reaction but had no therapeutic effect on the venereal warts.

Desensitization of Persons Subject to Ivy Poison. A successful method of protecting persons who are sensitive to poison ivy from attacks of dermatitis venenata would be hailed with delight by a great many individuals. Schamberg³ announces that he has now treated a score of susceptible patients, and all have remained free of dermatitis during the ivy season, whereas prior to undergoing this treatment they rarely escaped.

The method of treatment which he has been carrying out is as follows:

	c.c.
R Tincture of rhus toxicodendron.....	1
Rectified spirit	5
Syrup of orange, sufficient to make.....	100

The patient is instructed to take the mixture in half a glass of water after meals, as follows:

Breakfast, Drops	Lunch, Drops	Dinner, Drops
1	2	3
4	5	6
7	8	9
10	11	12
13	14	15
16	17	18
19	20	21

(2) Cor-Bl. f. schweiz. Aertze, Dec. 28, 1918.

(3) Jour. Amer. Med. Ass'n., Oct. 18, 1919.

When this dosage has been reached, for purposes of convenience and simplicity, the patient takes a *teaspoonful* in half a glass of water merely *once a day*. This should be continued throughout the ivy season.

The immunity (if one call it such) which is established after one month's administration will persist for about a month afterward. After this, susceptibility is likely to return.

The same mixture appears to exert a favorable influence on attacks of ivy poisoning in preventing an extension of the process, and in abbreviating the duration of the attack. In order to bring the patient more quickly under the influence of the drug, it should be given as follows:

Breakfast, Drops	Lunch, Drops	Dinner, Drops
2	4	6
8	10	12
14	16	18

Teaspoonful once a day, well diluted.

It is, of course, necessary to establish the fact that the ivy has been the cause of the dermatitis. *Rhus toxicodendron* tincture would probably be of no value in treating poison oak, primrose or other forms of plant poisoning.

The Etiology and Treatment of Seborrheic Eruptions. The widespread distribution and intractability of seborrheic eruptions among troops on active service led to the publication, by Barber and Semon,⁴ of some conceptions as to their nature and treatment.

The condition is very prevalent, and it may be said there is practically no skin disease in the army that is not complicated by seborrhea. The manifestations are protean, and include such apparently widely differing eruptions as a crusted and weeping eczema of the scalp, a dysidrotic eczema or cheiro-pompholyx of the fingers, and a patch of lichenification on the calf of the leg.

Darier, has correlated the tendency to seborrheic eruptions with a peculiar type of skin, to which he has given the name "kerose." Its clinical stigmata are briefly:

(4) Brit. Med. Jour., Sept. 7, 1918.

1. A brownish or dirty yellowish complexion.
2. Wide-mouthed and prominent pilosebaceous follicles, with hyperkeratosis of their orifices.
3. A slight thickening of the skin, with diffuse hypertrophy of the horny layer, and a tendency to fine desquamation. It is on this substratum or *terrain* that seborrheic manifestations most commonly appear.

In the first decade of life there may be pityriasis sicca of the scalp; toward puberty and later, seborrhea oleosa; from the fifteenth to twenty-fifth years we frequently find acne vulgaris, rosacea, and the so-called eczematides, whereas seborrheic alopecia takes its origin between the twenty-fifth and thirtieth years. The areas of the body affected are both diffuse and regional. The middle area of the face, the medi thoracic regions, the flexures of the limbs, and the pubic and internatal regions are peculiarly susceptible.

The etiologic factors, according to Darier, are two: sexual development, and erroneous diet in which excessive carbohydrates and stimulants, faulty mastication and constipation all play a part. Darier's conception has found many supporters. In his opinion, the bacteria described as specific by Sabouraud and Unna (and always met with abundantly in seborrheic lesions) owe their activity and pathologic effects mainly to the soil on which they are growing, which in its turn is dependent on the underlying constitutional state of the patient.

The frequent association of nasal and nasopharyngeal catarrh with the outbreak on the skin led to examination of a large number of cases: In fifty-nine out of ninety-three cases examined, posterior rhinoscopy revealed a yellowish mucopurulent secretion. The discharge varied in amount. In some cases the vault of the nasopharynx was coated, as if painted over with a scum-like mucus; in others, it was in amount sufficient to be expressed into the pharynx on exciting a forcible elevation of the soft palate. In twenty-four of these cases conditions of the nose and nasopharynx were demonstrated sufficient to warrant the supposition that a similar state of sepsis as in the fifty-nine already recorded had previously existed, and recurred from time to time.

There are in the collective experience of Barber and Semon two types mainly of seborrheic individuals:

1. Those congenitally predisposed, or who have acquired the tendency in infancy: These patients give a history of operations for adenoids, glands in the neck, frequent attacks of bronchitis and eczema in their childhood. They have thus in their youth conformed in all respects to the type of individual described by Czerny as exhibiting the "exudative diathesis."

2. Those in whom the state has suddenly appeared as the result of active service and its inevitable conditions: The affected individual of the second type develops symptoms for the first time on active service. An inquiry into his past history does not usually elicit a story of frequent colds or catarrhal attacks. The configuration of the upper respiratory tract is apparently normal, although there is often an associated subacute nasopharyngitis of the type noted as characteristic by Captain Jones-Phillipson. Prognosis is better in cases of this type, and relapse less likely to occur.

There is one feature which is common to both types of seborrheics, and that is a pronounced and remarkably constant hyperacidity of the urine. It was this association that first led to the assumption that the seborrheic state is really a manifestation of acidosis. It has been proved again and again that as soon as the urine becomes amphoteric or is made alkaline by the administration of drugs by the mouth, the acute stage of a seborrheic eruption comes to an end and the patient rapidly improves in health; and that, conversely, the urine is invariably acid at the onset of a relapse. The chemical examination of the urine, has never revealed the presence of diacetic or beta-oxybutyric acids, nor is it suggested that the degree of acidosis present at all resembles that commonly encountered in diabetes, but there are certain resemblances in the clinical features of the two diseases. The striking susceptibility in both to secondary infections, such as carbuncles and boils, the congested appearance of the extremities, the hyperacidity of the urine, and the reaction to treatment by alkalies, are worthy at least of cursory examination.

The chemical investigation of the condition of relative

acidosis in such cases is still incomplete; but one test suggested by A. W. Sellards, and considered by him to be the most delicate was applied to a large number of cases. This test consists in determining the "alkaline tolerance." The meaning of this phrase may be explained as follows:

The normal alkalinity of the blood depends on the existence in it of certain fixed bases, chiefly carbonates and phosphates; these are the so-called "buffer" salts. They combine with and partially neutralize acids; without their presence, acid by-products of metabolism—for example, CO_2 and lactic acid—would render the reaction of the blood so acid as to be physiologically intolerable. In a normal person with a sufficiency of these fixed bases in his blood and tissues, the intake of any appreciable quantity of alkali—for example, sodium bicarbonate—is followed by its immediate excretion in the urine. If, however, the fixed bases are deficient, additional alkali taken, instead of being excreted, is stored in the tissues and the urine remains acid.

Sellards has shown that 5 grams (about 75 grains) of sodium bicarbonate given by the mouth is practically the upper limit of normal tolerance. This amount is almost invariably sufficient to change the reaction of the urine of a normal person from acid to alkaline. In cases of acidosis very much larger quantities must be given before the reaction of the urine changes.

The formula adopted for the administration of the alkali was the following:

	gm. or cc.
Magnesium carbonate	
Calcium lactate	
Potassium citrate	2
Sodium bicarbonate	4
Chloroform water to make.....	30
	33

This is given in increasing doses until the urine becomes alkaline. In some cases as much as ten times the above amount will be required daily to change the reaction of the urine. As a result of the administration of the alkali two fundamental facts have been established:

1. The majority of patients with seborrheic mani-

festations show a markedly increased alkaline tolerance, many of them to an astonishing degree.

2. In nearly all cases, once the urine has been rendered alkaline, all active inflammatory processes cease, and the eruption rapidly clears.

After studying the effect of giving alkalis in some three hundred cases with seborrheic manifestations, the authors have satisfied themselves that the action of the alkalis may be described as specific. So constant is this phenomenon that it is almost always possible to predict with confidence that should a patient under alkaline treatment present new or active lesions (for example, eczema or boils), his urine will be found to be still acid; an increased quantity of alkali must therefore be given until the reaction of the urine changes. As might be expected, the lower alkaline tolerance the more rapid is the reaction to treatment, and the less the tendency to relapse.

It is contended that administration of alkalis abolishes the necessity for local applications, but it is claimed that this method of treatment hastens in remarkable fashion the clearing of the various eruptions dependent on the seborrheic state, and provided that the patient be then given an adequate quantity of alkaline salts *per diem*, relapses will not occur.

Alkali Reserve of the Blood in Diseases of the Skin.

The alkali reserve, consisting of bicarbonates, alkali-protein compounds, and small quantities of alkali-phosphates, maintains the plasma at a constant slightly alkaline reaction despite the fact that acid products of metabolism are constantly being passed into the blood. Under normal conditions, these substances are present in very constant quantities. A diminution in the alkali reserve is known as acidosis and may be recognized by a variety of clinical symptoms and by characteristic alterations in the composition of the blood, urine, and alveolar air.

Schwartz, Levin, and Mahnken⁵ studied the alkali reserve in the blood of a number of cases of cutaneous diseases. In this work attention has been almost entirely confined to the inflammatory dermatoses. On general principles it seemed more likely that an acidosis might be

(5) Jour. Cutan. Dis., September, 1919.

found associated with this group rather than with the dermatoses classed under the hypertrophies, atrophies, new growths, and parasitic affections.

The authors examined in all 139 cases of which eighty, or 59.7 per cent., gave normal values; fifty, or 35.9 per cent., gave values indicating a mild acidosis; five, or 3.5 per cent., values indicating a moderate acidosis, and one, or 0.7 per cent., showed a severe acidosis. This last was in a case of diabetes complicated with carbuncles.

[It would be interesting for the authors to investigate the alkali reserve of cases of seborrheic dermatitis, inasmuch as Barber and Semon (*vid supra*) found such a high alkali tolerance in their cases. Giving alkalies to their patients to the point of alkalization of the urine resulted in rapid healing.—M.]

ERYTHEMAS.

Endemic Erythema Multiforme. A definite cause may be ascribed to certain cases of the clinical entity that we call erythema multiforme. The rôle of certain drugs, antitoxins and serums has long been recognized. Cases developing following the ingestion of stale meat, fish and oysters, have been seen sufficiently often to warrant the assumption of direct causation, theoretically being due to the absorption of products of decomposition, bacteria or their products. Parker and Hazen studied a group of cases occurring in the course of such diseases as typhoid and diphtheria, and were inclined to favor a toxic theory. The theory of absorption of intestinal toxins has long been prominent in the literature. Lain, Chipman and others have recently associated erythema multiforme with focal infections about the teeth, tonsils and accessory air sinuses. Mahon, Vidal and others, from a purely theoretical standpoint, believed a number of cases to be of bacterial origin. Corlett reported a case following a gunshot wound in which a streptococcus was found. Epidemics have been reported by Gaul, Herxheimer, Dühring and others.

W. H. Guy⁶ reports an epidemic form of erythema

(6) Jour. Amer. Med. Ass'n., Dec. 14, 1918.

multiforme at Camp Travis, Texas, during the months of February and March, 1918. In all, forty-seven cases were seen. The cutaneous pictures varied through all grades with mild erythematous lesions to those showing all manner of individual lesions or a preponderance of vesicular and bullous lesions on the skin and the mucous membranes. In most of the cases with extensive skin involvement the onset of the disease was heralded by a mild chill or chilly sensations, followed by a febrile reaction that continued over a period of from fourteen to twenty-one days. The temperature curve was irregular, but showed a tendency to an evening rise and a morning remission, all ending by lysis. Many of the patients observed had a rise of temperature for two or three days only, the highest recorded temperature being about 100° F. Several had no abnormal temperature. There were purpuric lesions in approximately 10 per cent. of the cases. Only two gave a history of an attack prior to enlistment; ten of the forty-seven returned to the hospital with a second attack; and one with a third attack. Careful physical examinations failed to reveal anything noteworthy except that nearly all had hypertrophied and mildly inflamed tonsils. Several had open wounds, which were the result of recent vaccinations.

The laboratory findings showed all the urines to be practically normal. A few patients had transient albuminuria. The feces were negative. In the red cells of the blood there was no change; in the white cells, a moderate leukocytosis, rarely over 11,000. The hemoglobin was normal. The differential count showed that the leukocytosis was due to an increase in the polymorphonuclears.

Blood cultures taken at different times during the course of the disease, were all negative, as were cultures from vesicular and bullous lesions. Throat swabs showed all the organisms usually found. Cultures from deep tonsillar crypts showed in thirty cases a hemolytic streptococcus as the predominating organism. Superficial swabs were negative for this organism in the same cases. In nine cases a pyogenic streptococcus was found. In two cases in which the throat and tonsils were negative, the hemolytic streptococcus was isolated from recent vaccination wounds.

At the same time that the cases under consideration were being studied, there was in Camp Travis an epidemic of streptococcus respiratory infections, in the greater number of which *Streptococcus hemolyticus* was recovered.

Repeated attempts to obtain pure cultures of *Streptococcus hemolyticus* on defibrinated blood agar failed, and no growth was obtained on plain plus reaction agar. Serum from infected individuals did not agglutinate the organism.

It was noted that with the clearing of the exanthem the authors were unable to obtain the streptococcus with the same facility from the tonsil crypts, but that in the patients with second attacks the organism could again be formed. Believing that this organism was possibly the cause of this particular group of cases, acting by elaboration of toxins from a focus in the tonsils, all patients in whom the streptococcus was found were referred for tonsillectomy as soon as the exanthem and temperature had subsided. In none of these cases was there a recurrence.

Toxic Erythema. Bullous lesions in toxic erythemas are of not infrequent occurrence, and may offer great diagnostic difficulties, especially when one is called upon to make a differential diagnosis between eruptions of this type and a genuine pemphigus.

David Lieberthal⁷ gives a good exposition of the toxic eruptions in which bullous lesions occur. In administering drugs, especially iodine compounds, it is advisable to ascertain whether the patient is suffering from renal or cardiac insufficiency. Caution must be exercised in giving sedatives, and particularly hypnotics for the relief of severe itching which frequently occurs in the toxic erythemas. The drugs will relieve the symptoms temporarily, but with a cessation of the drug the itching not only will recur but will usually be greatly intensified.

An increased susceptibility to certain foodstuffs and to albuminous substances, which are produced within the intestinal tract, may be explained as the result of anaphylactic sensitization.

(7) Jour. Cutan. Dis., December, 1918.

DRUG ERUPTIONS.

Pigmented Erythematous Patches Recurring after Arsphenamin. Brocq has described erythematous patches which recurred *in situ* after the ingestion of antipyrine. Thibierge and Mercier⁷ describe a similar condition which recurred after each injection of novarsenobenzol. The first injection was given in 1918, during which year there were given thirteen injections in all. In January, 1919, the patient was given another injection and shortly afterward there appeared on the right lateral surface of the neck a red patch the size of a small coin which later became brown and remained a pigmented spot. In March this patient received another injection early in the morning and in the afternoon the same spot doubled in dimension and there appeared a peripheral zone of erythema which was less marked in the central area. In April another injection of the same dose was given and at this time an injection of adrenalin was also administered. The same spot reacted in the same way as after the preceding injections.

Dermatitis Medicamentosa Due To Antipyrine, With Persistent Pigmentation. Although cases of dermatitis medicamentosa following the ingestion of antipyrine have been reported, in some of which pigmentation has ensued, nevertheless the case reported by Norman Paul,⁸ on account of its clinical characters and the somewhat permanent nature of the pigmentation, is worthy of record. The patient was a male, aged 32 years, a strong and healthy individual, who has reached some prominence in the athletic world. He had already consulted numerous men and, uncertain of the diagnosis, they usually fell back upon the possibility of the eruption being syphilitic, an opinion which was causing him considerable uneasiness of mind.

The patient stated that it had been four or five years since the eruption first appeared, but that he had been unable to suggest any causative factor, although the relationship of drugs to the cutaneous lesion was suggested by the author. However, during the time that the

(7) Bull. Soc. franc. de dermat et de syph., Nos. 3 and 4, 1919

(8) Med. Jour. Australia, February, 1919.

PLATE I.



Warts resulting from inoculation.—Wile and Kingery, page 6.

man was under observation fresh lesions appeared and again being questioned as to whether any medicine had been taken, he stated that he had taken some headache powders (antipyrine) the previous evening. This incident recalled to his mind the fact that the first eruption had also followed closely upon the taking of a headache powder and was associated with intense pruritus, so severe that the surface epidermis over the affected patches was excoriated by rubbing. The patient was then unable to tolerate his clothes, on account of the resultant tenderness and was compelled, in order to avoid dressing, to spend a couple of weeks at the seaside. The quantity of antipyrine taken was not ascertainable.

The lesions were all isolated and sharply defined plaques; the recent ones were erythematous, circular, well-defined, slightly elevated and appeared mainly on the extensor surfaces of the arms in the vicinity of the elbows and on the buttocks. They were itchy, and were for the most part the size of a shilling or a sixpence (approximately the size of a quarter and a dime). The older lesions, which had already been present for some considerable time before examination, were flat, definitely circular and varied in size, the majority being approximately the size of a half-dollar. They were divided into two zones, an external, of a dark, purplish or violaceous color, with a central whitish area, suggestive of and giving the appearance of fine atrophy. Other lesions again showed the outer zone to be of a slaty-brown color with a similar white center; in appearance they were not unlike lesions sometimes seen in macular leprosy. On the anterior surface of the body there were only two lesions, one above the umbilicus, the other affecting the greater portion of the penis and showing a dark purple or blackish tinge, without any central whitish area, and of an irregular shape. If antipyrine powders were taken within an hour these old lesions again became itchy.

Brocq and Darier have reported cases of persistent erythema, accompanied by pigmentation and produced by antipyrine. Fournier reported pigmentation of the penis following an erythematous eruption after taking antipyrine, and Ehrmann noted macular pigmented lesions on the penis and scrotum which recurred in the

same place from time to time and usually followed the ingestion of antipyrine. In the present case it is suggested that the pigmentation was in a measure due to the severe rubbing and excoriation of the lesions, as others not so severely dealt with disappeared without leaving any signs of pigmentation.

URTICARIA.

Febrile Urticaria. Two unusual cases of severe urticaria, reported by Captain Lawrence,⁹ occurred in the British Station Hospital, Nowshera, N. W. P. India, within a week of each other, and were also identical in the type and duration of the disease. Both were characterized by a severe and generalized urticarial eruption, five days pyrexia, and the absence of any of the usual exciting causes of urticaria or inherent tendency to the disease.

The first case occurred in a soldier, under treatment for right empyema by drainage of the pleural cavity. The discharge had practically ceased, and the man's temperature had been normal for a fortnight, when one morning he complained of itching of the left buttock, where several typical urticarial wheals were to be seen. Next day the wheals appeared on his forehead, and the lips were so swollen that he could hardly open his mouth. On the third day the eruption was generalized, and practically the whole body was covered with patches of elevated wheals surrounded by an area of congestion less raised than the wheals themselves (Fig. 1).

Pyrexia began on the second day, and reached its maximum when the eruption was worse. The pyrexia and the urticaria declined and disappeared *pari passu*.

Neither dietetic changes, drugs, vaccines, insects nor any of the usual exciting causes could be traced in this case. No other symptoms or signs of disease were present, except the almost cured empyema. The man had never had an attack of urticaria before and felt quite well as soon as the eruption passed off. He was treated at first with calomel and salines and afterward

(9) Brit. Med. Jour., June 7, 1919.

with cooling applications, sedatives, and hypnotics, but obtained little or no relief from the intolerable itch.

The second case occurred in a medical officer, working in the same hospital, but not in attendance on Case 1. He was in perfect health when he noticed one morning five days later a small white wheal on his forehead, which rapidly grew to the size of a hen's egg; he also felt itching on the parts of his back and shoulders exposed to the friction of clothing. By next day the eruption had broken out in patches over most of his body, but the size of the swelling and the intensity of the itch in any one part was not always the same. On the

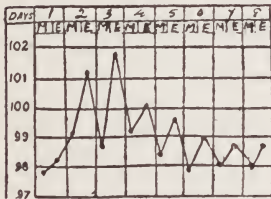


Fig. 1 — Rash appeared on the first day, was at its worst on the third day, and disappeared on the sixth.

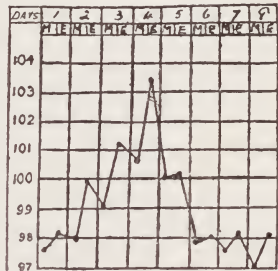


Fig. 2 — Rash appeared on the first day, was at its worst on the fourth day, and disappeared on the sixth.

fourth day of the eruption the temperature was 103° F. and the urticaria and swelling at their worst. After that the eruption rapidly declined (Fig. 2).

The mucous membranes were not affected, nor was there any sign or symptom of disease elsewhere. The pulse throughout was of a rate commensurate with the temperature. It was easily compressible and bounding, but not dicrotic. The urine was normal; there was no jaundice and the blood count showed a slight polymorphocytosis of 77 per cent. but no eosinophilia.

Treatment was commenced with purgatives. Calcium lactate was given in full doses and adrenalin chloride hypodermically. Cool alkaline baths and sponging, $\frac{1}{3}$ grain doses of morphine, full doses of bromides, were

all tried to allay the intolerable itch, but with no success. The patient was driven to walking about in pajamas in the cold night air, and found that the best way to allay the itching was to keep himself almost shivering with cold.

Again in this case no exciting cause could be found. He had never suffered from such a condition before, but had noticed in the last six months one or two sudden transient attacks of edema of the nasal mucous membrane with complete stoppage of nasal respiration. Apart from this he had never had any sign of vasomotor weakness or instability.

Urticaria Pigmentosa with Hypertrophy of the Liver and Splenomegaly. Certain authors, Darier in particular, believe that urticaria pigmentosa is in some way due to gastro-intestinal or hepatic disturbances. In the opinion of Jeanselme and Touraine,¹ researches directed to these features of urticaria pigmentosa may shed some light on the etiology of the disorder. In 1913, these authors reported the case of an infant aged 20 months who, in the course of development of urticaria pigmentosa, presented a myeloid reaction of the type of Jaksh and Luzet without splenomegaly. Earlier, Bizzozero reported a similar case with micropolyadenopathy. Casar in 1917 published a report of another case which also presented myeloid deviations. The patient whose case is reported by Jeanselme and Touraine was a man 40 years old who had had urticaria pigmentosa since the age of 15. The dermatosis had occurred in successive attacks of from three to six weeks each. The lesions first appeared on the arms, then on the trunk and later on the face. At no time had the condition been pruriginous. The patient stated that he had been troubled with digestive disorders since 1912. The dermatosis was typical of urticaria pigmentosa and consisted of macules or papules which, after friction, showed the typical urticarial reaction. Physical examination showed a large abdomen without ascites. The liver was lower than normal and hypertrophied. The spleen was greatly enlarged and occupied the major portion of the abdomen;

(1) Bull. Soc. franc. de dermat. et syph., Nos. 3 and 4, 1919.

it measured 20 cm. in its greatest diameter and 15 cm. transversely.

The blood was carefully studied; the examinations showed that the globular resistance was greatly lowered and the coagulation time much increased. Enumeration of the cells showed 3,195,000 red cells and 3,400 leukocytes. Spinal puncture gave a negative fluid but the Bordet-Wassermann test on the blood was positive. Unfortunately, there was no histologic examination and the presence or absence of mast cells was not determined. The man was treated with radiotherapy, but received no antisiphilitic treatment.

[As is well known, the infantile types of urticaria pigmentosa, as a rule, have a typical histologic picture in which the most characteristic feature is the large number of mast cells present with a tendency toward arrangement in chains. We have studied several cases of the adult type of urticaria pigmentosa in which these mast cells were lacking and in which there was no apparent systemic disturbance of any kind. It would seem that histologic examination of this case and observation of the results of intensive antisiphilitic treatment should be reported before placing the case definitely in the category of acquired urticaria pigmentosa.—M.]

Urticaria Pigmentosa. A case of urticaria pigmentosa presenting no evidence of hepatic, gastro-intestinal or myeloid changes, is reported by Montpellier.² The child was 6 years ago, of excellent antecedents and, so far as could be determined, in a splendid state of health. All the various laboratory tests were negative. A biopsy showed a typical urticaria pigmentosa picture with mast cells present. The mast cells were so thick in places that they presented the picture of the *Unna mastzellen* tumor. The only positive findings of any kind in this patient consisted of a positive tuberculous cutaneous reaction without any clinical evidence of tuberculosis, and an eosinophilia of 7 per cent. The author believes that the two types of histologic pictures, namely, the mast cell tumor and the disseminated mast cell lesions are to be explained on the basis of the lesion which has

(2) Ann. de dermat et de syph., September, 1918.

been selected for biopsy; whether it be an active lesion which has first been irritated and has become edematous, or whether it is an inactive lesion which has not undergone the formation of the edema in the process of urtication.

DERMATITIS.

Chronic Suppurative Acrodermatitis. This disorder has been intensively studied by many workers but as yet no one has evolved a thoroughly satisfactory method of treatment. Dubreuilh³ reports in detail three cases which he treated with radiotherapy with results that he considers entirely successful.

The term *acrodermatite suppurative continue* was first applied to the dermatosis by Hollopeau. Dubreuilh prefers the adjective pustular rather than suppurative because in his experience the essential lesion has been a pustule although in one case vesicles occasionally occurred. He objects to the term *phlycténose récidivante des extrémités* used by Audry because it does not indicate the pustulation which is always present and, moreover, the process is continuous rather than recurrent.

Dubreuilh makes no attempt to explain the mode of action of the Roentgen ray in these cases because neither one of the two theories—nervous and infectious—proposed for acrodermatitis is confirmed by the results of treatment. It is an interesting fact that in all three of the author's cases radiotherapy led to a peculiar reaction. The skin became markedly edematous, of a deep wine-red color, and spotted over with numerous punctiform, intra-epidermic hemorrhages. The corneous layer then became lifted by the thick, spongy, edematous mucous layer of the skin. After the degeneration had taken place, a thin new epiderm formed but the pustules did not recur.

Oil Dermatitis. Last year Thibierge⁴ described a follicular, pustular, pigmented dermatitis of the exposed

(3) Ann. de dermat et de syph., December, 1918.

(4) Practical Medicine Series, 1918, Vol. VII., p. 104.

areas in munition workers. Hudelo and Barthélémy⁵ have studied the case of a woman 46 years old whose work consisted of handling and checking shells. On the dorsal surfaces of the hands and forearms and exposed regions of the neck and on the face the skin was uniformly colored and had a nutmeg-grater-like keratosis. There was a marked pigmentation which was most pronounced about the pilosebaceous orifices. The authors believe that the pigmentation was due to the steel dust held in suspension in the oil and actually rubbed into the skin, just as in tattooing. Thibierge was of the opinion that the pigmentation in his case was an intra-dermic pigmentation of inflammatory origin.

Ragweed Dermatitis. The list of substances and plants which may produce a dermatitis in susceptible persons is a long one and is constantly being lengthened. A group of four cases of dermatitis produced by coming in contact with ragweed is reported by R. L. Sutton.⁶ All the patients were men who had severe and persistent dermatitis for a few months during the ragweed season. Three were treated with ragweed pollen with good results.

Dermatitis due to French Gas Masks M-2. An acute and severe dermatitis apparently resulting from contact for a period of 20 minutes with a gas mask containing sodium hyposulphite was observed in the French army by Lahernadie.⁷ Marked edema, vesication and crusting occurred. After the condition had yielded to treatment, contact with the same mask and later with sodium hyposulphite produced a similar eruption. It was necessary to supply the patient with another type of mask.

[A chronic dermatitis on the hand of photographers is common. This is probably due in large part to the fixing solution of sodium hyposulphite rather than to the developer, except in those individuals who are especially susceptible to metol hydroquinone and pyrogallol.—M.]

(5) Bull. Soc. franc. de dermat. et de syph., 1919. Nos. 5 and 6.

(6) Jour. Amer. Med. Ass'n., Nov. 8, 1919.

(7) Ann. de dermat. et de syph., December, 1918.

Genital Yperite Burns Simulating and Masking Syphilis. Gas burns in general and those of yperite in particular were very frequent on the external genitalia during the last months of the war. In some cases these burns were limited to the genitalia. Occasionally the burns simulated syphilis, particularly in the beginning, and led to diagnostic difficulties. The difficulties were intensified because the men were inclined to ascribe all lesions of the genitalia to gas burns. Gougerot and Clara⁸ describe a series of cases in which syphilis was both simulated and masked by the action of yperite. There were two series of cases. In one there was no lesion outside of the external genitalia. The patient as a rule had come in contact with gas and carried it to the external genitalia from his fingers while urinating. The very delicate skin of the prepuce was promptly burned by the very short contact of the exceedingly small quantity which might be transferred from the fingers. The cornified palmar surfaces of the hands and fingers, on the contrary, were not injured by the small amount of yperite they came in contact with.

In the second type, the burns were generalized and existed on other parts of the body as well as on the external genitalia, but the genital lesions were much more slow in healing and remained ulcerated long after the burns on the body had healed. In such cases it was necessary to determine whether syphilis actually existed.

Inflammatory burns of the glans and the shaft of the penis resulted in a phimosis, or a paraphimosis with voluminous edema. The secondary preputial inflammation set up led to inguinal adenopathy, and in such a case the picture was that of a chancre, and laboratory methods became necessary to establish a diagnosis. The antecedents, and associated symptoms, the negative results of the search for *Spirochaeta pallida*, the absence of a positive Bordet-Wassermann reaction, the appearance of the cicatrix and the evolution all permitted of a positive diagnosis being arrived at. Occasionally, however, the burns and a chancre might co-exist, and in such cases

(8) Ann. des mal. vén., May, 1919.

it was very important that the burns be not allowed to obscure the presence of a syphilitic infection.

One such case is reported in detail. Syphilis was suspected but the patient denied all exposure and the anti-septic treatment which he had received prior to coming under the observation of the authors rendered the search for *Spirochaeta pallida* futile. Eventually, the syphilitic infection was recognized and treatment instituted.

Genital Yperite Burns. Out of a group of 441 cases of yperite burns Clerg, Guilhaume and Rosselot⁹ observed nine cases in which there were very serious genital lesions. As a rule, the burns are very superficial and heal without leaving anything more than pigmented traces. Occasionally, however, a considerable destruction of a tissue occurs. In the first twenty-four hours there appears a very painful edema with phlyctenules which pass rapidly into suppuration. The penis becomes very turgescient and takes on the appearance of the tongue of a bell. Added to this is the intense swelling of the prepuce, phimosis or paraphimosis, a marked purulent secretion covering the glans, and painful micturition. This leads at once to a tentative diagnosis of venereal disease.

The evolution of this burn was always slow. The swelling persisted for many days and the ulceration led to intense pain. Slowly the edema retrogressed, suppuration ceased and after one or two months approximate healing had occurred. The cicatrization, however, renders the phimosis particularly rebellious because of the retraction of the tissue and because of the production of fibrous adhesions.

Relation of Thyroid to Infantile Eczema. Believing that dysthyroidism in the lactative mother may be the etiologic factor in the production of infantile eczema, Ravitch and Steinberg¹⁰ call the attention of dermatologists to the advisability of investigating the functioning of the thyroid in all such cases. No data is offered in the support of their theory.

(9) Progrès méd., Sept. 6, 1918.

(10) Jour. Cutan. Dis., May, 1919.

TUBERCULOSIS.

Tuberculosis of the Skin. A group of papers on tuberculosis of the skin was read before the Section of Dermatology of the American Medical Association at the 1918 meeting in Chicago. The papers making up the symposium, which was opened by Sigmund Pollitzer¹ appear in the *Journal of Cutaneous Diseases*.

The papers, and the discussion which followed, disclosed the fact that dermatologists are far from being agreed on many questions concerning tuberculosis of the skin and particularly on the status of the tuberculide; according to some men the term tuberculide should not even be retained. Pollitzer, however, believes that the conception of the group of tuberculides served a valuable purpose in stimulating study and discussion of the subject, though the tendency today is to use this term for all tuberculous processes in the skin in which tubercle bacilli have been found, in analogy to the term syphilide for cutaneous lesions in which spirochetes are present. We recognize today a large and protean group of diseases which are distinctly of tuberculo-bacillary origin, either direct or hematogenous; and a second group of which we can say that they seem to bear some relation to tuberculosis, but the proof of this relation is still lacking.

The only absolutely diagnostic feature of a tuberculous process in the skin as elsewhere is the demonstration of tubercle bacilli, either by histologic or cultural methods or by animal inoculation, or by the occurrence of a distinct focal reaction after tuberculin injection. The histologic structure of the lesion is by no means diagnostic. The classic picture of tubercle as described by Virchow—lymphoid, epithelioid or giant-celled—establishes a certain degree of probability of the tuberculous nature of a given process; but on the one hand this picture may be absent in a definitely tuberculous lesion, and on the other a variety of non-tuberculous lesions, such as leprosy, syphilis and sporotrichosis, may present the same picture.

(1) Jour. Cutan. Dis., February, 1919.

Far from producing a single typical reaction in the tissues, the tubercle bacillus may occasion a variety of lesions which are very different histologically. In the ulcerating tuberculous lesions of the mucosa, for instance, where tubercle bacilli are commonly present in great abundance, the usual picture is simply that of diffuse granulation tissue. The reaction of the tissues—sclerosing, exudative, elephantiasic or keloidal processes—varies with the number and virulence of the germs and the resistance of the individual, wherein the different factors grouped under the term immunity come into play.

In a tuberculous lesion of the skin, changes in the tissues often occur at points situated at considerable distances from the location of the bacilli—changes produced apparently by the action of diffused tuberculo-toxins. To what extent, if any, the circulation of such toxins derived from a visceral focus of tuberculosis plays a rôle in the causation of some dermatoses frequently associated with visceral tuberculosis is still a moot question.

A probable diagnosis of cutaneous tuberculosis will rest on (1) the sum total of clinical and microscopic characters, (2) history of the case, and (3) the general condition of the patient. For the proof of the tuberculous nature of such a lesion we must demand the demonstration of bacilli, or at least a clear focal reaction after tuberculin injection.

In accordance with the foregoing, the following dermatoses are recognized today as tuberculous: *Lupus vulgaris*, *lupus miliaris disseminatus*, *tuberculosis verrucosa cutis*, *scrofuloderma*, *erythema induratum*, *subcutaneous sarcoid*, *tuberculosis ulcerosa*, *acute miliary tuberculosis*, *lichen scrofulosorum*, and *papulonecrotic tuberculide*.

In a second group of dermatoses the relation to the tubercle bacillus may be said to be a matter of suspicion, but the proof of this relation has not been established. The most important members of this group are *multiple benign sarcoid*, *lupus pernio*, *lupus erythematodes*, *granuloma annulare* and *diffuse exfoliating erythro-*

derma. It will be the work of the future to clear up the relations of these dermatoses to the tubercle bacillus in the skin or tuberculous process in the viscera.

“Tuberculous” Purpura Erythema Multiforme and Erythema Nodosum. The tendency of recent advances in the study of the etiology of dermatoses has been, increasingly, to show that many supposed clinical entities, so styled on purely morphologic grounds, have a multiple etiology. One of the conditions undergoing such etiologic revision is the erythema group, including the clinical entities of erythema multiforme and erythema nodosum. The work of revising our outlook on erythema multiforme, purpura and urticaria was well begun by Osler in 1895. Erythema nodosum is of particular interest because on its border lie erythema induratum and the group of dermatoses designated after Darier as “tuberculids” whose intimate relation to tuberculosis is now generally accepted. Erythema nodosum, in the opinion of J. H. Stokes,² is in a fair way to be at least partially allied to this group, and it awaits only a sufficient body of clinical evidence and some corroborative work to establish its connection.

One of the very interesting features of the etiologic developments concerning erythema nodosum is the demonstration by Rosenow, in 1915, of a polymorphous Gram-negative diphtheroid as the cause of the condition. This organism, whose infection-atrrium is apparently the tonsils and pus pockets about the teeth, gives rise especially to the more acute types of the disease. The pathology of erythema nodosum, however, is such that it seems a rash assumption to attribute the changes to a single type of organism. There would appear to be no reason why embolic infarction or thrombosis of terminal vessels in the skin of the extremities, and varying grades of exudation and inflammatory reaction about the affected vessels, could not be produced by living tubercle bacilli in a hypersensitive individual, as suggested by the studies of Rist and Rolland; or by the dead bodies or the “toxins” of the same organism, as suggested by the experiments of Chauffard. While with a larger experi-

ence we may come to recognize clinical differences between erythema nodosum produced by the tubercle bacillus or its products and that produced by the Rose-now diphtheroid, or perhaps by streptococci, the assumption that the pathologic differences between the various types will be striking and pathognomonic is in the present uncertain state of knowledge gratuitous. It seems not unlikely that the clinician who ascribes too high a degree of etiologic specificity to a condition such as erythema nodosum will fail to recognize many important relations of the picture and will overlook other etiologic possibilities which may be of the greatest import to the particular case. The ten cases which form the subject of this report in contrast with a number of those reported in the literature occurred in adults. The youngest patient was 16, the oldest 43; the majority over 25.

The clinical picture of tuberculous purpura, tuberculous erythema multiforme and tuberculous erythema nodosum is made up of objective rather than subjective symptoms. Estimated by a rigorous standard, four of the first eight cases were positively demonstrated as tuberculous, and the remaining four were of a highly suggestive character if not absolutely definite. Two additional cases of erythema nodosum, morphologically conforming to the conventional or rheumatic type, were also suspected of being tuberculous and are under observation. Of the eight original cases, the tuberculous focus in four was identified by pathologic examination; two were positive and one indeterminate in the roentgenogram of the chest; four showed physical signs in the lung and one was indeterminate, and four had visible and palpable adenopathy. No evidence of syphilis could be identified in any of the ten cases; two of the patients had tuberculides of the papulonecrotic and erythema induratum type; and one of them had folliclis, a tuberculide of the fingers; three presented purpuric lesions, three had lesions of the erythema multiforme type and six had nodular lesions of the type encountered in erythema nodosum, though of varying grades of acuteness and severity. In two of the cases of nodular erythema the onset was that of erythema nodosum and

the localization approached that of erythema induratum. In one of these cases the nodose lesions were associated with a typical erythema induratum with ulceration.

The consideration of the possibility of a septic focus in these cases was of interest. In one of the patients the tonsils did not seem involved; in two they were mildly septic but not markedly affected; a fourth with markedly infected tonsils had them removed without appreciable effect on the process and two developed their first attack, one of erythema nodosum and the other of folliculitis, three and four years after the removal of the tonsils. Whereas gross examination for an alveolar or gingival focus was negative throughout the series of ten cases, in one suspected case the patient had an alveolar abscess demonstrable by the radiogram; two cases were negative. Radiograms of the teeth were not taken in the remainder. The secondary focus of pyogenic or diphtheroid infection seems to be a negligible quantity in this group, although its importance is much more apparent in a review of the entire series of tuberculids; four in ten had symptoms of a rheumatic character, in the form of myalgia, arthralgia and neuritis. The modes of onset in the ten cases were slight sorethroat in two, cold and grippe in two, typhoid, so-called, in one and by indefinite non-localizing symptoms or the typical abrupt onset of erythema nodosum in five. The part played by the respiratory atrium is much more apparent in the larger series. Dermatologically the differentiation of tuberculous from streptococcus or diphtheroid erythema nodosum can scarcely be worked out on so small a group of cases. A tentative personal view of the matter is as follows: Although the two conditions are at times indistinguishable from each other on the score of acuteness, localization and course, and this fact cannot be too forcibly emphasized, the following table embodies the main points of difference as the writer has seen them:

**Streptococcus Erythema
Nodosum.**

Nodes larger, more edematous, and brawny, more tense, and hemorrhagic. May reach the size of a small palm.

**Tuberculous Erythema
Nodosum.**

Nodes smaller, less marked peripheral reaction, hemorrhagic changes less marked. In their place may be purplish lividity, but usually only a well-developed erythema.

Greater involvement of the superficial tissues.

Distribution more apt to be over the front of the lower extremities, especially below the knees and over the front of the thigh; also around the larger joints.

Color changes, more marked than in the tuberculous type. The brown element especially marked. Behaves typically like a bruise.

Symptoms in general more severe, progress more rapid, whole process more acute, tendency to self-limited course.

Nodules more circumscribed and deeper.

May appear on either front or back of the leg, but tends to localize posteriorly. May appear in smaller numbers or in crops or groups, or one or two on the upper extremities. May appear on the feet.

The nodule is paler at the onset, and progresses from pink to a livid purple or bluish tinge. If it persists (as erythema induratum) it remains bluish, softens and may show a bullous surface or undergo necrotic sloughing. The nodules may present only a mild erythema which subsides, leaving no color changes or only a faint yellow stain, or there may be colorless ones among the erythematous nodes, suggesting Wende's nodular tuberculosis of the hypoderm.

Process more indolent, lesions less tender or even painless, more persistent, may last months or longer, especially if there is little inflammatory reaction. Of material assistance in diagnosis is the concomitant occurrence of an indubitable tuberculide, such as folliclis, or the papulonecrotic types of lesions or their scars.

Multiple Disseminated Lupus Vulgaris. Hazen³ describes two interesting cases of disseminated lupus vulgaris which came under his observations, and gives a review of the previously reported cases.

For years, clinicians have realized that pulmonary tuberculosis, especially in children, was likely to be first noted after one of the exanthems, especially measles. It is generally conceded that even active pulmonary tuberculosis is due primarily to bacilli that have been carried

(3) Jour. Cutan. Dis., February, 1919.

through either the blood-stream or lymphatics. In the case of multiple lupus it is at once obvious that external infection can not be considered and we are forced to conclude that the lesions are of embolic character. It is true that many cases of lupus vulgaris are apparently due to direct external infection, but in certain other instances this can not be satisfactorily proved, and it is highly probable that many of the cases of lupus are due to emboli.

It has generally been believed that tuberculosis verrucosa cutis is due to external infection, but the cases cited by Bourgeois and others would seem to indicate that this form may also be of embolic origin.

There is often a typical clinical picture: A child has an attack of either measles or scarlet fever; about the time that the rash begins to fade, or a few weeks thereafter, a crop of red papules appears, and persists, although the child seems perfectly well. In going over the literature of the condition Hazen collected sixty-four cases, in many of which, however, the notes were fragmentary, inasmuch as the cases were shown at the various society meetings. In this series there were twenty-six males and thirty-four females, whereas in four instances the sex was not stated.

The pre-existing disease was found to be measles in forty-one instances, scarlet fever in six, varicella in one, influenza in one, tuberculous glands of the neck in one, unmentioned in eleven, and absolutely denied in three.

In seventeen instances the lupus appeared before the rash had faded and in twenty-two other cases it developed within four weeks. The type of eruption was papular in thirty-seven cases, verrucose in fourteen, psoriasiform in three, ulcerative in one, nodular in one, and mixed in six. The lesions varied in number from 150, in the case of Philipppson, to a comparatively small number. In the majority of instances there were from twenty to thirty lesions.

The face was involved thirty-four times, the scalp twice, the neck in nine instances, the trunk in twenty-five times, the arms forty-seven times, the legs in forty-one instances, the elbows and knees four each, the hands

PLATE II.



Sarcoid on the right cheek. Diffusely infiltrated, elevated and livid red.—Sweitzer and Michelson, page 37.

ten times, the feet three times, the buttocks eight times and the genitalia twice.

Miliary Tuberculosis of the Skin, Lichen Scrofulosorum and the Papulo-Tuberculosis. The tuberculous diseases of the skin with their polymorphous manifestations may conveniently be grouped under three heads. In the first group are placed the dermatoses occurring as single or isolated lesions, such as lupus vulgaris, tuberculosis verrucosa cutis, scrofuloderma, and ulcerating forms of cutaneous tuberculosis. The second group comprises the exanthematic forms, represented by miliary tuberculosis of the skin, lichen scrofulosorum, the papulo-necrotic tuberculides, erythema induratum and the sarcoids. In the third group are included the dermatoses of which the tuberculous etiology is still uncertain; these are lupus erythematosus, lichen nitidus, certain forms of exfoliating erythrodermas and erythemas and the cutaneous manifestations of lymphadenosis and Hodgkin's disease. Of these three groups Wise⁴ confines himself to a consideration of the second or exanthematic forms of eruption, namely, miliary tuberculosis, lichen scrofulosorum and the papulo-necrotic tuberculides.

When Darier formulated the term "tuberculide" he had in mind a group of dermatoses which occurred only in tuberculous subjects, without, however, revealing within the lesions the presence of tubercle bacilli, or even the anatomic changes characteristic of tuberculous processes in the tissues. These eruptions usually made their appearance in crops; the lesions were symmetrical in distribution, more or less disseminated over various regions of the body; they were benign, showing no tendency toward local extension and usually healed spontaneously. They were thought to be provoked by the toxins of the tubercle bacillus, thus explaining the negative findings with regard to tubercle bacilli in the lesions, at the same time suggesting the reason for the relative mildness of the affection and its tendency toward spontaneous healing, as compared with true tuberculosis of the skin. In other words, the tuberculides were regarded in the light of a toxicoderma. In support of this view,

(4) Jour. Cutan. Dis., February, 1919.

it was discovered that the subcutaneous injection of tuberculin would sometimes result in the appearance of lesions closely resembling the papulo-necrotic tuberculides. This toxin theory was strongly favored by Boeck, Hallopeau and Klingmüller and was soon amplified by another conception which suggested the possibility that the tuberculides were actually provoked by tubercle bacilli, but that the latter occurred as attenuated or even dead organisms.

Today it is assumed by many men that isolated tubercle bacilli are directly productive of the papulo-necrotic tuberculides. The bacilli may gain entrance into the circulation in scant numbers, but in virile form; they ultimately reach the integument where they are subjected to various antibodies of the organism and there may undergo lysis, thus setting free certain toxins which are instrumental in the provocation of the papulo-necrotic lesions. The bacilli are readily destroyed in the skin, as that organ is known to be unfavorable soil for their growth; the conditions of immunity which permit the existence and multiplication of the bacilli in the internal organs, seem to be inactive in the skin. In the latter organ they readily become a prey to the antibodies, more especially as the bacilli are assumed to be in a state of diminished virulence and subject to various other factors unfavorable to their growth; among these are the cellular immunity against certain organisms, said to be inherent in the tissues of the skin itself, and the inimical influence of the small lipase content of the skin.

Miliary tuberculosis of the skin is provoked by the dissemination of tubercle bacilli in the blood-stream—it is a hematogenous infection. The disease is rare. Among thirty-two infants afflicted with tuberculosis, Tileston found seven presenting miliary cutaneous lesions a very large proportion, compared with the findings of other writers. Lenier and Spieler also reported an unusually large number of instances and believed that the eruptions were probably overlooked both by the layman and the pediatrician. However that may be, the disease is certainly uncommon in this country. The

eruption usually manifests itself after an attack of scarlatina or measles, in infant life. A few cases in adults have been recorded (Naegeli, Hedinger and Nobl). It may appear in association with generalized miliary tuberculosis, or it may constitute the first prodromal symptom of that disease. From the prognostic standpoint the appearance of the eruption is a serious manifestation because the infants thus affected often succumb to tuberculous meningitis.

Lichen scrofulosorum affects chiefly children before puberty, but numerous cases are reported occurring in adult life. The older patients almost invariably present evidences of active tuberculous processes, usually of benign character, such as chronic glandular and bone affections; advanced pulmonary tuberculosis is rare. The eruption often follows an attack of measles or scarlatina. It may persist for months without causing discomfort and may scarcely attract the patient's notice. The lesions may disappear spontaneously without leaving any traces on the skin, or small macules, light brown in color, may remain after their involution; in some instances, small round, punched-out scars are left.

An analysis of the different factors which play a part in the pathogenesis of these three tuberculous affections of the skin, leads one to the conclusion that the toxic theory in the sense of a toxicoderma—is, in the light of modern knowledge of immunity processes, no longer tenable. These dermatoses have ceased to be “tuberculids” and have emerged from the obscurity which that vague term implies, to take their places in the category of “tubercloses.” Papulonecrotic tuberculide has become *tuberculosis papulo-necrotica*; lichen scrofulosorum has become *tuberculosis lichenoides*. If we were to concede that the term “tuberculide” is strictly analogous to the term “syphilide,” any reference to a change in nomenclature would be uncalled for; nobody doubts that a syphilide is still a syphilide, whether or not the microscope reveals *Spirochaeta pallida* in its substance; the same is true of a lepidid. In accordance with modern conception, a lesion may still be the result of a tuberculous process in the skin, whether or not the

bacillus of tuberculosis can be demonstrated in it. The characteristic histologic tuberculous nodule is evoked, not by the presence and multiplication of the tubercle bacilli *in situ*, but rather by the destruction of the bacilli under the influence of antibodies; for it has been shown (Lewandowsky) that when the bacilli are growing and multiplying in the tissues, unhindered by antibody substances in the organism, the result is a tissue reaction in the form of non-specific, ordinary inflammatory changes; under such circumstances, too little time has elapsed to permit of the production of sufficient antibodies to hinder the action of the bacilli. But when a sufficient amount of antibody substance is available, the blood-borne bacilli are gradually destroyed on their entrance into the skin, and only then are they capable of giving rise to the so-called tuberculoid tissue changes, or tuberculous nodules.

The variations in the form and type of eruptions provoked by the tubercle bacillus seem to depend, therefore, on three chief factors: (1) the individual disposition of the patient; (2) the number of bacilli circulating in the blood-stream and (3) the degree of immunity reaction residing in the affected organism.

Dermatoses Possibly Related to Tuberculosis. After a careful review of the literature Scheer and Lane⁵ have come to the conclusion that there is little evidence in support of the theory that lupus erythematosus is a tuberculous process.

The relation between the exfoliating erythrodermas and tuberculosis has been thoroughly reviewed by Lewandowsky. The association of pityriasis rubra of Hebra with tuberculosis has been described by Jadassohn, Kanitz, Poland, Foster, O. Miller, Halle and others. The only authentic case, however, is that described by Bruusgaard. This was a case of exfoliating erythroderma associated with universal tuberculosis of the lymph glands in which typical tubercles were present in the skin; typical bacilli were found in these tubercles. A case of Finger and Wertheim, and one of Koyptowski and Willowilyski showed a tuberculoid structure of the

(5) Jour. Cutan. Dis., February, 1919.

skin. But the majority of the cases of exfoliating erythroderma have shown no evidence of tuberculosis of the skin; and the disease, like lupus erythematosus, is probably a skin reaction to some toxin, tubercle or other. Of the dermatoses possibly related to tuberculosis, lichen nitidus alone shows a typical tuberculous structure. Evidence of associated tuberculosis—tuberculin reaction, tuberculous glands and other signs—has been furnished by the cases of Kyrle, Sutton, and Lewandowsky. Arndt found Much's granules. But animal experiments have been negative and the clinical appearance of the lesions, their long duration without change, certainly do not suggest tuberculosis. Owing to the rarity of the disease there have not been sufficient studies of late years to add to the remarks of Lewandowsky in his review.

Sarcoid of Boeck and Erythema Induratum. In 1914 Sweitzer⁶ reported a case of sarcoid of Boeck and gave a review of the literature. Sweitzer and Michelson⁷ have observed another case and have compared the findings with those of several cases of erythema induratum.

They were impressed with the strong resemblance of the histologic picture of a subcutaneous sarcoid, with that of a case of undoubted erythema induratum. The sections were identical except that the one from the sarcoid was a growing tumor with vigorous cells and the one from the erythema induratum case had cells that were undergoing retrograde changes. Both sections revealed the same type of cells and both looked like tuberculosis (Plate II).

In the first case of Sweitzer's the patient gave a positive animal inoculation showing a small tubercle. The present case failed to give positive animal results, but the histologic picture strongly resembled that of a tuberculous infection as also did the roentgenogram of the chest. The relatively small number of animal inoculations that have been positive is probably due to the fact that if the disease is tuberculous, the bacilli may die out or be attenuated and fail to give a positive take. The fact that the patients are often robust is of no signifi-

(6) Practical Medicine Series, 1914, Vol. IX.

(7) Jour. Cutan. Dis., February, 1919.

cance either way, as we often see patients with lupus vulgaris who are quite healthy otherwise.

From an extensive study of the literature and of these two cases, the authors are of the opinion that sarcoid of Boeck is due to tuberculosis. They admit that a difference of opinion still exists among some writers. Several have attempted to class it as related to syphilis. It is easily differentiated from syphilis microscopically, but some cases have responded to arsphenamin; this is not surprising as tuberculids often respond to arsphenamin.

Darier in 1910 in an excellent article divided the sarcoid group into four classes:

1. Multiple, benign sarcoid of Boeck.
2. Subcutaneous sarcoid of Darier-Roussy.
3. Erythema induratum-like sarcoid of the extremities.
4. Spiegler-Fendt type: non-tuberculous, composed of round cells.

Instead of simplifying the subject, this classification has only added to the existing confusion. Type 4 belongs to the neoplastic lymphoderma and can be definitely dropped as having no connection with sarcoid of Boeck. Type 3 is probably erythema induratum. Types 2 and 1 are one and the same and show the variety of ways in which sarcoid of Boeck can manifest itself.

In both of the authors' cases of Boeck's sarcoid, they find a subcutaneous sarcoid along with other manifestations. In the case under consideration, the subcutaneous lesions corresponded clinically with the subcutaneous sarcoid of Darier-Roussy; they occurred along with lesions of the diffuse, infiltrating type. The writers maintain that sarcoid of Boeck is a form of tuberculosis of the skin, and should be classed as such.

Sarcoid of Boeck has been said to respond to arsenic. In their two cases, this was not true. Both Fowler's solution and neo-arsphenamin (neosalvarsan) were given to the patient whose case is the subject of this report and with no results. Tuberculin was tried and was of no value. Freezing with carbon dioxide snow

had been tried previously, but evidently without enough pressure and time allowance.

The Diagnostic and Clinical Aspects of Tuberculides. The material of an intensive study made by J. H. Stokes,⁸ consists of thirty cases of the so-called papulonecrotic tuberculides, of erythema induratum, and of associated conditions constituting, according to the most widely accepted explanation the allergic response of a hypersensitized skin to emboli of tubercle bacilli from a tuberculous focus elsewhere in the body.

The author suggests that internists and general diagnosticians should find it worth while to familiarize themselves with the essential lesion of these types of tuberculides, which may prove of great assistance in the recognition of obscure tuberculosis.

The tuberculide when not ignored by the general diagnostician is usually confused, as shown by this series, with acne and furunculosis, with syphilis, especially if the Wassermann be positive and, on the legs, with acute surgical conditions and ulcer varicosus. Therapeutic tests for syphilis with arsphenamin are misleading in these cases. The diagnostic import of the lesions in obscure lymphadenitis is at times overlooked.

The association of these lesions with tuberculosis in this series was evidenced by a family history in one-fourth of the cases, incontestible objective signs in more than half (57 per cent.) and presumptive signs of the disease in 70 per cent. One-third of the patients had radiographic signs of pulmonary tuberculosis; an equal number had suggestive or positive physical signs of lung involvement. The importance of lymphatic involvement is illustrated by the fact that two-thirds of them had a tuberculous lymphadenitis.

The type and location of the focus of tuberculosis do not seem to influence the tuberculide beyond the marked association with glandular involvement. On the other hand, the influence of vascular abnormalities and chronic passive congestion in the extremities is very apparent; 96 per cent. of the lesions involved the extremities. Lesions appeared on the ear in 13 per cent.

(8) Amer. Jour. Med. Sci., March, 1919.

Slight fever at onset, loss of weight which occurred in 40 per cent., amenorrhea in 43 per cent. of the women, moderate leukopenia, slight but occasionally severe anemia, and vernal periodicity are the significant signs. An onset and course marked by rheumatic symptoms is very common (46 per cent.) and often misinterpreted. The recognition of the focus of tuberculosis must depend largely upon objective evidence. There was a notable absence of cough, sweats and hemoptysis. Patients of florid, seemingly robust type are not infrequently subjects of tuberculides.

Evidence of the importance of a septic focus and collateral types of infections appears from the history of tonsillitis in 39 per cent., "rheumatism" in 46 per cent., pneumonia in 26 per cent., grippe in 54 per cent., and pleurisy in 18 per cent. These conditions seemed frequently to stand in direct predisposing or exciting relation to the tuberculide. A total of 70 per cent. had symptoms and findings suggesting the presence of a septic focus, and 62 per cent. had had significant respiratory infections excluding pleurisy.

While no direct relation of the tuberculide to the clinical condition of the tonsils could be established, 50 per cent. of the patients had markedly septic tonsils, the remainder were passable and none normal. Examination of the teeth by x-ray in a limited number of the latter cases demonstrated the presence of septic foci in 45 per cent. of nine patients. Other foci should be searched for. While the secondary or septic focus was obviously present its influence is obscure. Removal of the tonsils in seven cases failed to prevent the outbreak of a tuberculide or modify its course, and complete extirpation of all recognizable septic foci in two cases, without removing or treating the tuberculous focus, was also unavailing.

It is conceivable that the effect of a secondary septic focus, while not direct, is predisposing in that toxins or even bacteria emanating from it may be in part responsible for the cutaneous allergy which is presupposed in explaining the pathogenesis of the papulonecrotic tuberculide. Evidence of the ability of a septic focus to

produce or predispose to dermatitis, urticaria and similar expressions of cutaneous hyperirritability are accumulating. Further indirect evidence of a possible peculiar allergic state of patients with tuberculides is found in reported and personally observed cases of non-specificity in their Wassermann reactions and in their hypersusceptibility to arsphenamin.

Circinate Tuberculous Lesion Simulating a Syphilide.

A circinate arrangement of lesions is usually considered as an important diagnostic element in the recognition of cutaneous syphilitic lesions. Pinard⁹ had the opportunity of seeing two cases in which there were cutaneous lesions having a circinate arrangement strongly suggestive of syphilis. The first patient was an officer of infantry who had a large lesion on the right buttock in the form of a "C." The papules which constituted the lesion were markedly infiltrated. They were dark red and scaling, and there were present many scars marking the sites of former active lesions. Carefully controlled Bordet-Wassermann reactions were negative before and after treatment. The lesion resisted two series of intravenous arsphenamin injections. The guinea-pig inoculation of material taken from a tumor mass in the hypochondrium was positive for tuberculosis.

The other case occurred in an artilleryman, who had a circinate arrangement on the left buttock. The Bordet-Wassermann was likewise negative both before and after arsphenamin treatment.

PITYRIASIS ROSEA.

Pityriasis Rosea Considered as a Tuberculide. In support of his contention that pityriasis rosea is a tuberculide, P. Le Damany¹ offers the following proof:

1. Pityriasis may recur.
2. Frequency and importance of symptoms of systemic disturbances which may precede, accompany or follow the eruption.

(9) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(1) Presse méd., March 10, 1919.

3. Micropoly adenopathy of long duration usually present.

4. Frequent coëxistence of diverse manifestations of tuberculosis.

5. Positive tuberculin reaction.

Two cases of recurrence of the disorder are cited, and a few cases in which a positive skin test or an elevation of temperature with tuberculous infections are reported.

[Typhoid fever may recur but that does not prove that typhoid fever is therefore tuberculous; recurrence of pityriasis rosea is one of the rarities in dermatology. The infectious exanthemata also have systemic disturbance but no one claims that therefore they are tuberculous. The presence of discrete or diffuse adenopathy proves nothing because it may be found in many patients if careful search be made. Moreover, the von Pirquet test is positive in practically every person over 14 years of age. Lastly there is no reason why tuberculous patients should not have pityriasis rosea as well as other individuals who are free from the disease.—M.]

Pityriasis Rosea of Gibert. The etiology of pityriasis rosea remains obscure. Two cases of this disorder reported by Pinard² are of interest, because they both occurred in syphilitics. The first case was found in a man 30 years old and was remarkable for its unusual duration of six months. Moreover, after the lesions had yielded to treatment pigmented areas persisted for some time. General examination of the patient was negative. The second case occurred in a man with a chancre of five days' duration. The pityriasis rosea eruption had appeared only a few days before the onset of the chancre.

Dubois has reported the finding of a parasite in the squams of pityriasis rosea, but this organism could not be grown artificially. Brocq is of the opinion that pityriasis rosea is an infectious pseudo-exanthem of internal cause. Sabouraud believes that it is an erythema analogous to erythema multiforme. Gougerot maintains that it is a cutaneous manifestation of an undetermined systemic intoxication. Damany believes that pityriasis

(2) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

rosea is a tuberculide. There is very little evidence, however, to support this contention. Pinard has frequently observed pityriasis rosea in patients with pulmonary or lymphatic tuberculosis.

After the presentation of this paper before the society Simon stated that he had observed what might be considered an epidemic of a dozen cases of pityriasis roséa in the same region in the environs of Paris. In his opinion, the co-existence of pityriasis rosea and syphilis in these two cases was merely incidental. Brocq stated that he had frequently observed pityriasis rosea during the evolution of syphilis. Also, he frequently encountered the disorder in patients who were suffering from systemic disturbances. He rarely encountered it in subjects who were otherwise perfectly well.

LEPROSY.

Juxta-Articular Nodule in a Leper. A disease occurring in certain parts of the tropics, notably in New Guinea, Java, Siam, Algiers, Senegambia, Madagascar, New Caledonia and French Guiana, has been described by several authors under the title of "Juxta-Articular Nodules." The accounts of these cases state that the lesions are subcutaneous, hard, painless, round or irregularly-shaped nodules, usually located near one of the joints, especially the ankles or knees.

The case of a leper presenting these nodules is reported by D. H. Currie and H. T. Hollman³ of the U. S. Leprosy Investigating Station. The patient was an Hawaiian, male, 46 years of age. Although his clinical symptoms were such as to leave little doubt that he was suffering from the nerve type of leprosy, the bacillus of Hansen had not been demonstrated. Both of the nodules were located on the left lower extremity; one just over the outer maleolus and the other on the anterior aspect of the ankle at a level with the first. The lesion over the maleolus began six years ago and was approximately 1 x 1 cm. in area and about 1 cm. in elevation above the surrounding normal skin. The second lesion began

(3) New Orleans Med. and Surg. Jour., March, 1919.

thirty-six years ago. At the end of five years it had reached the size of a pea, while ten years from the time it was first noticed it had attained its full development; since then it has remained stationary in size. The tumor has never been painful and until recent years it has not caused the patient any inconvenience, since, in the early part of his life, he went barefooted. One of the nodules was excised and from the cut surface a mold was grown. This mold, belonging to the genus *Aspergillus*, at first occurred as a white, slowly-extending carpet over the surface of the medium; later it assumed a dark green hue, and finally turned violet in color. After one or two generations it grew readily on all the ordinary laboratory agar media, including the more ordinary sugar agars. It grew rapidly at incubator temperature only, and did not grow at all below 56° C. The changes in appearance and color of the mold were identical with that of *Aspergillus fumigatus*, as was its behavior in regard to temperature, with the exception that, instead of changing from a dark green to a snuff color at the time of maturity, it turned to a dark violet, as mentioned above. It differs from *Asperigullus fumigatus* in apparently not being pathogenic to guinea-pigs, although the inoculated animals are still under observation. In this respect it resembles the fungus mentioned by Fontoyont and Carougeau, but they were unable to say whether or not it is identical.

Microscopically, it was found that a great mass of the tumor was composed of dense, fibroconnective tissue. The structure was not, as some have described in their cases, arranged concentrically, nor was there observed either a central or an outer zone of different make-up. There was no suspicion of caseation in any part of the specimen, but scattered here and there, in the most irregular manner, were numerous small arteries and veins, with their walls greatly thickened, and surrounding each of these small vessels there were irregularly-shaped areas, which showed round-cell infiltration, as well as the presence of large lymphoid cells and spindle cells in places where organization of the connective tissue had begun to take place. A few other large cells, suggestive of giant cells, were observed occurring in nests containing several

of these large cells surrounded by fibrils of connective tissue. Neither acid-fast nor other bacteria were observed in the specimen, with the possible exception that in the inflammatory areas there were a few slender, branching fibers, which suggested some of the higher fungi; but on this point the authors could not be certain. No mold spores were seen in the tissue.

Interstitial Absorption of Bone in Leprosy. The osseous mutilations in leprosy may take place in several ways. Necrosis and elimination of the sequestrum through perforating ulcers is the rule. A case in which there was complete absorption of the metatarsal bone without elimination of the sequestrum is reported by Dubreuilh.⁴ The metatarsal bones of the left foot disappeared, leaving nothing but their proximal epiphyses. The articular surfaces appeared normal, but the bone was drawn out to a fine stylet and ended in a point. The bone apparently had disappeared by a simple process of interstitial absorption.

MILITARY DERMATOSES.

Dermatology in the Army. An unusual opportunity is afforded, says W. H. Guy,⁵ for the study and treatment of dermatoses in the army, because, probably for the first time in his experience the dermatologist has been able to control his patients. Troops are inspected at regular intervals and men found with skin lesions are referred for diagnosis and treatment. An out-patient department and a ward in the base hospital are set aside for the care of dermatologic cases, and only cases of certain types are admitted to the hospital. The acute exanthemas are isolated and held during the usual quarantine periods. All aggravated skin diseases and all parasitic infections are admitted to the hospital. In the early days of this work, such diseases as scabies and the various vegetable parasitic infections were healed in the out-patient department, but such a high percentage of recurrences and so many instances of spread of diseases were found that it was decided to hold all such cases in the hospital until not only was the patient cured, but

(4) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(5) Jour. Cutan. Dis., April, 1919.

his clothing and bedding were sterilized. Since that time there has been little trouble in controlling these infections. The following table shows the diseases treated:

Acne	60	Lichen chronicus circum-	
Acne varioliformis	1	scriptus	5
Blastomycosis	1	Lichen planus	1
Bromidrosis	10	Lipoma	7
Burns	19	Lupus erythematosus	2
Carbuncle	16	Lupus vulgaris	1
Cheilitis exfoliativa	1	Lymphangioma circum-	
Clavus	12	scriptum	1
Cornu cutaneum	1	Miliaria (severe)	150
Dermatitis exfoliativa	1	Molluscum contagiosum ..	2
Dermatitis factitia	2	Paronychia	5
Dermatitis herpetiformis..	3	Pediculosis capitis	80
Dermatitis acute infectious		Pediculosis corporis	103
eczematoid	2	Pediculosis pubis	50
Dermatitis medicamentosa	5	Pellagra	4
Dermatitis, occupational..	20	Pityriasis rosea	39
Dermatitis papillaris cap-		Pityriasis versicolor	65
illitii	3	Pompholyx	5
Dermatitis venenata	36	Pruritus cutaneus	4
Dermatitis seborrheica...	1	Pruritus ani	4
Ecthyma	5	Psoriasis	20
Epidermolysis bullosa her-		Purpura, symptomatic	7
editaria	2	Scabies	947
Epithelioma	5	Scleroderma	1
Erythema multiforme	68	Sycosis, staphylococcus ...	36
Erysipelas	75	Tinea circinata	210
Erythema nodosum	2	Tinea unguis	4
Erythema pernio	1	Tineas cruris	120
Erythema toxicum	5	Tinea tonsurans	3
Favus	1	Tuberculide, papulonecrotic	1
Furunculosis	65	Ulcer, traumatic	72
Glossitis areata exfoliativa	8	Ulcer, varicose	15
Granuloma pyogenicum ..	1	Urticaria	70
Herpes zoster	23	Varicella	26
Herpes simplex (severe)..	38	Variola	27
Hydroa vacciniiforme	1	Verruca	3
Hyperidrosis palmaris ...	4	Vitiligo	1
Ichthyosis simplex	4	Fibroma molluscum	2
Impetigo (Bockhart)	10	Xanthoma tuberosum mul-	
Impetigo contagiosa	35	tiplex	1
Keloid	3	Xeroderma pigmentosum..	3
Keratosis palmaris and			
plantaris	3		

[During a period of eight months one of us (M) had an opportunity of observing the dermatoses among the men passing through the demobilization station at Camp

Funston, Kans. The most common disorder observed was eczema marginatum, or ringworm of the crotch. In some organizations as high as 25 per cent. were infected. The next most common affection was scabies. In one group of overseas men, 10 per cent. had aggravated cases. Pityriasis versicolor was very common and most cases had apparently gone unrecognized. A few had been given treatment for "liver spots" with cathartics and tonics. Acne of the face was rare although quite common on the back. Xerosis, in various degrees of severity, was observed almost daily and apparently caused the men no inconvenience. All the psoriasis cases seen were mild and many of them had been recently cleared with chrysarobin ointment.—M.]

Chronic Skin Affections in the Soldier. From an examination of almost 8,000 men at the mustering office, and from a large experience in the dermatologic wards of the base hospital at Camp Lee, C. J. Hailperin,⁶ has been impressed by the potential and actual loss to the military service in accepting men who are suffering from chronic or recurrent dermatoses.

There are many types of skin affections which in ordinary civil life are of comparatively little significance. Many men go through life with these troubles without suffering any great inconvenience. When these men enter the Army, however, and are subjected to the physical and mental strain incident to Army life, they begin to have an aggravation of their trouble. They soon become incapacitated for work, and are sent to the infirmary or hospital for treatment. Many of these patients improve under rest and proper care, only to relapse soon after their return to duty. A sick or disabled man is a tax on the military organization. He can not work; he requires medical attention, and to that extent he is a liability rather than an asset.

The accompanying table gives the various types of dermatoses as found among approximately 8,000 white men within a few days after their arrival at Camp Lee. Incidentally, this table also gives the number of men found with open syphilitic lesions, such as chancres, mucous patches and condylomas.

(6) Jour. Amer. Med. Ass'n., Nov. 2, 1918.

DERMATOSES AMONG EIGHT THOUSAND MEN

Acne keloid	1	Ichthyosis	8
Acne pustulosa	75	Lupus vulgaris	1
Acne rosacea	1	Parapsoriasis	1
Alopecia areata	8	Pediculosis corporis	1
Cysts, sebaceous (scalp)...	3	Pediculosis pubis	3
Canities	2	Pityriasis vericolor	109
Dermatitis venenata	1	Psoriasis	40
Eczema chronic	16	Pupura	2
Erythrasma	2	Scabies	20
Eczema seborrheic	18	Syphilis (open lesions)...	125
Folliculitis	11	Trichophytosis corporis ...	3
Erythema multiforme	4	Ulcer, varicose	2
Lipomas	4	Urticaria	5
Herpes zoster	2	Urticaria pigmentosa	1

Many of these diseases are of little significance from the standpoint of military service. Eczema however gives considerable trouble, particularly if it affects the lower extremities. Among the men examined were many who gave a history of chronic eczema, but who did not show any active manifestations. Active military life causes a return of their trouble, and they must then be sent to the hospital for treatment.

Microbic Dermoepidermites in War. The "*dermo-épidermites microbiennes*" are traumatic cutaneous infections, particularly epidermic, which ordinarily extend over a large surface with a multiform appearance and are due to pyogenic organisms, particularly streptococcus or staphylococcus, usually to the association of the two. Gougerot⁷ emphasizes the importance of the recognition of these cases and says that a great many men were incapacitated for military service for months because of the failure of medical officers to make the correct diagnosis. Once the diagnosis has been arrived at and proper treatment instituted the cases, as a rule, rapidly clear up. Gougerot classifies these cases into four groups:

1. Suppurating types: (a) Types having innumerable purulent vesicles; (b) exulcerating types; (c) erythemato-squamous impetiginous types; (d) a follicular-pustular type; (e) a type complicated with ecthyma; (f) ulcerating types without ecthyma.

2. Weeping, erosive, eczematous cases.

3. A dry, squamous type.

(7) Bull. Soc. franc. de dermat. et de syph., 1919, No. 1.

4. Polymorphous type made up of all four types.

Scabies in Military and Civil Life. The incidence of scabies has been a little more than 5 per cent. of the total dermatologic cases observed by F. C. Knowles⁸ during the last fifteen years. During twelve months' tenure at a large British general hospital there were somewhat more than 2,000 cases treated in the skin department and of this number over 500 were scabies. If conditions secondary to scabies, such as furuncles, impetigo, folliculitis septic sores and so-called inflammation of connective tissue (I. C. T.) were included, almost 1,000 more of these cases would be classified under the former heading. In other words, 1,500 of the 2,000 dermatologic cases were either frankly scabies or secondary to scabies.

TABLE 1.—DIFFERENTIATION BETWEEN SCABIES AND PEDICULOSIS CORPORIS

Scabies.	Pediculosis Corporis.
General in distribution, exclusive of the face and scalp.	General in distribution, exclusive of the face, scalp, hands, feet and the lower arms and the lower legs.
Predilection for the webs of fingers, flexure surface of the wrists, penis, flexure surface of extremities, and anterior surface of trunk.	Predilection for extensor surface of the upper arms and upper legs, and posterior surface of the trunk, particularly across the shoulder and lower back.
Diagnostic sign the "burrow," a minute zigzag line, consisting of alternating blackish and whitish dots, the width of a thin thread, and from the smallest fraction to $\frac{1}{8}$ inch in length; itch mite too small to look for; pinpoint in size.	Diagnostic sign the pediculus, small pinhead in size, found in the seams of the clothes more frequently than on the body.
The eruption we speak of as multiform; papules, vesicles and pustules, boils and large crusts.	The eruption consists chiefly of long, linear scratch marks, small punctate hemorrhages and excoriations; not infrequently crusts and boils.
Itching severe, usually at night.	Itching severe, usually at night.

(8) Jour. Amer. Med. Ass'n., Nov. 16, 1918.

Table 1 will elucidate the differentiation clearly between pediculosis corporis and scabies. Scabies in military and in civil practice differs considerably as shown by Table 2.

TABLE 2.—SCABIES IN CIVIL LIFE AND IN MILITARY LIFE

Scabies in Civil Life.	Scabies in Military Life.
Eruption usually on the lateral aspect and webs of fingers, consisting of pustules and burrows, excepting in those unusually cleanly, in washerwomen, and mechanics who work in oils, greases, graphite, etc.	Hands are involved in but few cases.
Penis frequently shows only one or two pustules and burrows and occasionally none.	Penis usually shows a marked involvement, numerous pustules and burrows.
Complications are absent in most cases.	Complications, such as an unusually large number of pustules, boils, impetigo, and the so-called I. C. T. (secondary pustular lesions) are frequently present.

Scabies is readily differentiated from pediculosis for in the latter disease the diagnosis is based on finding the small pinhead-sized ovum ("nit") attached to the hairs in the pubic or axillary regions; in hairy individuals, any hair on the entire surface of the body, exclusive of the scalp may show this nit. In a recent series of 200 patients minutely examined, pediculosis pubis was present in 190 of the cases.

The method of treating scabies consists on the first day of giving the patient a warm bath with plenty of soap. One rubbing is given with sulphur (precipitated sulphur, 1 dram to the ounce of petrolatum) and on each of the next three days a sulphur rubbing is given. On the fifth day the patient is given a warm bath with plenty of soap followed by clean clothes.

Thorough and minute examination of the entire body is made to insure that no active disease remains. If active lesions are still present, four more days of sul-

phur rubbing are given, followed by another warm bath, another careful examination of the skin surface, and clean clothes.

There is no more efficient remedy for the treatment of all secondary pustular conditions following scabies than ammoniated mercury ointment, from 20 to 40 grains to the ounce of petrolatum. Boils in their incipience are best cured by rubbing in thoroughly each day for ten minutes a 25 per cent. ichthyol ointment; in a later stage they require opening. If boils continue to recur or a large number are present, autogenous vaccines are indicated. Septic ulcer and inflammation connective tissue not infrequently require rest in bed and the local application of ammoniated mercury, 20 grains to the ounce of zinc oxide ointment.

[A great many of the troops passing through the demobilization station at Camp Funston during the winter of 1918-19 were infected with scabies. In some organizations the percentage of infected men reached 11 per cent. The galleries were found most frequently between the fingers and on the penis and the cases did not differ in this respect from those seen in civil practice. The cases differed, however, from those seen in France in that these men had been inspected and the cases having the most extensive involvement had been eliminated, leaving only those cases which had few lesions or which had developed lesions *en route* from the points of debarkation.—M.]

Atypical Scabies. Typical scabies with "runs" is usually found over the front of the wrist and adjoining palm and between the fingers; the classic eruption occurs in this situation and over the elbows, in the axilla, over the abdomen, in the gluteal folds, in the male on the penis and in the female on the nipples. With its history of contagion and the involvement of the sleeping companion and of the family, and the bitter complaint of nocturnal itching, it is easy of recognition. The obscure, atypical cases, however, and they are not so infrequent, are very elusive, and because scabies is seldom cured unless recognized and never spontaneously dies out, may constitute a really grave malady from nervous exhaustion and want of sleep.

D. W. Montgomery⁹ describes the case of a young woman who had a minutely vesicular eruption on the interdigital surface of the fingers, some scratch marks on the arms and in the axilla, a finely granular crusted eruption in the supramental groove and an intense pruritis. A diagnosis of scabies was easily arrived at by shaving off the roof of a vesicle and demonstrating the parasite.

[As repeatedly mentioned in the editorial comment in these volumes, the only certain way of determining the presence or absence of scabies is by microscopic examination. By this means the editor has been able to find the acarus in both of two new vesicles, the only lesions present on the body of a young woman who had been exposed to scabies and who had sought medical advice soon after the exposure.

In the Army, there seems to have been a lamentable failure on the part of medical officers to recognize scabies, judging from the large numbers of infected men who passed through the demobilization camps. All these men were sent to the base hospital, carefully treated, their clothing sterilized, and returned to their homes free from contagion. At Camp Pike, during the assignment of the editor, no apparent attempt to treat these men was made. The weights and measures of the men were carefully made and tabulated, but cases of ringworm and scabies by the thousand passed through the station and were returned to civil life to infect the civil population. As a result of the carelessness of medical examining board of the Army, ringworm of the crotch and scabies will be disseminated throughout the nation, and will cause great discomfort in the civil population for years to come.—M.]

Atypical Localization of *Pediculus Pubis*. A rich man, 86 years old, who had had a generalized itching eruption for two years was seen by Dubreuilh.¹ He had consulted a great number of physicians without obtaining relief. When he consulted Dubreuilh he was told to strip for examination and immediately it was found that he was alive with pediculi. The hair of the

(9) Jour. Cutan. Dis., May, 1918.

(1) Ann. de dermat. et de syph., July, 1919.

entire body was covered with ova and the organisms were present in great numbers. Both the eggs and organisms were present in the eyebrows, in the scalp and in the mustache. The entire body was markedly excoriated and the examination was hastily brought to a close for the sake of the carpet. Local applications led to prompt relief and he returned in three weeks with no signs of the eruption but the ova were still present.

The author observed another man, 35 years old, who was a man of means, refined in his habits and excessively fastidious about his person. He was a syphilitic and in the course of injections of grey oil the author discovered a few lice in the region of the pubes, which disappeared under calomel and naphthol. A few weeks later the patient called the attention of the author to itching in the region of the mustache, and on examination Dubreuilh found a number of very small pediculi of the pubic type.

An Interesting Reaction to Louse Bites. Although the clothes louse is a known carrier of typhus and recurrent fevers and has recently been shown to be a carrier of trench fever, there seems to be no record that it may produce an illness due to a toxin or toxins introduced by its bite. Observations made by W. Moore¹ while attempting to raise large numbers of lice for experimental purposes during the spring of 1918 indicate that a severe intoxication may result in persons bitten by large numbers of lice.

Experiments were begun on the louse problem in the spring of 1917, with lice collected from the clothing of men in a municipal lodging house. They were kept in an electric incubator, heated to from 28° to 30° C. (82.4 to 86 F.). At first attempts were made to feed them on rabbits, guinea-pigs, monkeys and pigs; but they refused to feed on either the rabbit or guinea-pig, and while they attempted to puncture the skin of a young pig, they were unsuccessful. The lice fed on the monkey but they did not appear to thrive, which fact, together with the difficulty of so securing the monkey that it

(1) Jour. Amer. Med. Ass'n., Nov. 2, 1918.

was unable to interfere with their feeding, caused a discontinuance of these methods. A laboratory assistant then undertook to feed them on his arm. Local irritation from the bites made it necessary to invite others to assist in feeding the lice.

The author started feeding from 700 to 800 twice a day. Almost immediately a general tired feeling was noticed in the calf of the legs and along the shin bones, while on the soles of the feet and underneath the toes this tired feeling was so intense as often to prevent sleep until late in the night. An irritable and pessimistic state of mind developed. May 7, an illness resulted with symptoms very similar to grippe, and a rash similar to German measles was present, particularly over the shoulders and abdomen. As German measles was prevalent in the community at that time, it was considered German measles; and after remaining in bed for several days, he returned to work and again took up the feeding of the lice. The general feeling, previously noted was present with increasing intensity. By May 15, the number of lice in the reserve stock had increased to about 1,200 and May 28, the writer was again forced to remain in bed. The family physician was called and diagnosed the case as possibly grippe. The next day he was again called since a distinct rash was present all over the body. The rash was considered quite typical of German measles, but other symptoms of measles were absent. The heart was normal, the pulse about 90, and the temperature varied from 100 to 102° F. A blood count revealed a normal number of leukocytes and red corpuscles. A severe headache was experienced, accompanied with pains in the legs, not only along the shins, but also in the calf of the leg and the soles of the feet, while intense pain was present in all the joints of the body. The appetite was lost for several days, and the tongue was heavily coated. Dr. A. D. Hirschfelder, who had been assisting on the louse problem, saw the patient at this time and considered that it was not German measles, nor was it grippe, but might be trench fever. Glandular enlargement was absent and no enlargement of the spleen was noted. Recovery was complete except for a general weak condition by June 4.

In order to determine the rôle played by the lice, the feeding was resumed on two subsequent occasions with the same results. After the cessation of feeding and a period of two days spent in outdoor sports all symptoms disappeared.

EPIDERMATOMYCOSES.

Trichophytosis Capitus due to *Microsporon Lanosum* in Algiers. In 1907, Kopp stated that *Microsporon audouini* did not exist in Algiers, or at any rate that it was so extremely rare that it had not been encountered. In 1917, Brault and Viguiet stated that in twelve years' experience in Algiers they never had seen a case of this type of ringworm. After a study of fifty-four cases of trichophytosis, the organisms of which were all identified by culture, Montpellier and Lacroix² came upon a case of trichophytosis capitis which was carefully studied and found to be due to *Microsporon lanosum*. The child was 9 years old, was a native of Algiers and had never been away from the immediate vicinity of its home. There were no other similar cases in the neighborhood, and the child had not come in contact with animals about the house. The authors conclude that Algiers is particularly free from trichophytosis of the Gruby-Sabouraud type and that this was an infection of animal, and not of human origin.

Favus in an Adult. The statistics compiled by the American Dermatological Association show that favus is a rather rare disease. The disease occurs in only about 0.35 per cent. of all dermatologic cases and, furthermore, the patients are for the most part foreign-born. Stout reported a case in 1908 of generalized favus, involving the scalp, arms, legs, and nails in a native-born American.

The case reported by Charles Wolf³ is that of a soldier, 28 years old, born in Oregon. As far back as he could remember he had had trouble with his scalp. At the age of 14 the patient entered upon a seafaring life,

(2) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(3) New York Med. Jour., Aug. 30, 1919.

in which he continued until the outbreak of the war. On questioning whether other members of his family had had the disease, the answer was negative. The patient had sought treatment in civil life for favus, but was discouraged over the inability of physicians to cure him. For the last four years he had had no treatment, having decided to allow the disease to take its natural course.

This condition passed unnoticed when he enlisted in the army, for he allowed the hair of the unaffected part to grow luxuriantly, thus concealing the disease area fairly well. However, at one of the monthly physical inspections the regimental surgeon discovered the condition and the soldier was sent to the Walter Reed General Hospital, where he came under the observation of the writer. On examining the scalp one immediately noticed the abnormal length of the hair. Spreading the tufts of hair apart, the scalp showed confluent patches of thick, heaped up, crusted scales, grayish yellow in color, with typical scutella interspersed. There were small atrophic areas over the vertex resulting from the destructive action of *Achorion schönleini*.

The diagnosis of favus was made clinically and confirmed by microscopic examination. A not infrequent occurrence is the absence of any musty straw, mousy, or any other abnormal odor, often stated as being characteristic of favus. In this case the patient presented no odor whatsoever. No other part of the general surface showed any lesions, but the patient stated that he had several circinate lesions at various times on the back of the neck just below the hair line. These healed spontaneously and were in all probability favus lesions.

The patient at first refused radiotherapy, but later gave his consent to the x-ray treatment and received one epilating dose, measured by a Holzkecht radiometer. These areas subsequently cleared up completely, leaving a perfectly bald head. New hair appeared and the soldier was returned to duty.

Favus Herpeticus, or Mouse Favus. Last year S. N. Paul⁴ reported the occurrence of a widespread epidemic

(4) Practical Medicine Series, 1918, Vol. VII, p. 119.

of a skin disease among the mice found in the granaries of Australia. As a result of handling the wheat in which these mice had been feeding, a number of workers had been infected with a dermatosis which was shown to have been of murine origin.

In spite of the shortage of shipping, the United States has been importing considerable quantities of Australian wheat. The question arises: Is there danger that men engaged in the handling and milling of the wheat may become infected with this skin disease? In an attempt to answer this query, certain studies by R. E. Buchanan⁵ have been made at the Hygienic Laboratory of samples of wheat and of mouse skins collected in Australia by agents of the U. S. Department of Agriculture.

There seems to be some question as to whether the organism isolated by Paul, and named by him *Tricophyton rodens*, is the same as the fungus that causes mouse favus. The description and illustrations of Lawrence, on the other hand leave little doubt that he is dealing with *Achorion quinckeanum*. According to Paul, the characteristic skin lesions occur mostly on the exposed parts of the hairy regions of the face, producing a multiple kerion. In the particular case described, two months had elapsed between the opportunity for infection and the development of the lesions. Lawrence believes that Paul was not dealing with a typical case. Fungi isolated by the latter author both from field mice and from man showed the cultural characteristics of the mouse favus fungus, and identical lesions were produced in mice and guinea-pigs inoculated with cultures from each source. The lesions in man show well-developed scutula in some cases, and correspond accurately to the description of the favus herpeticus of Quincke.

From the review of the literature by the author, it is evident that a distinct disease, mouse favus, exists commonly in Belgium, England, France, Germany, Italy, Scotland, Switzerland, probably other parts of Europe, and Australia, and abundant evidence of the transmissibility of the disease from mouse to man, producing the favus herpeticus of the glabrous skin. It is apparent

(5) Jour. Amer. Med. Ass'n., Jan. 11, 1919.

that the disease is of sufficient importance to warrant the careful study of the possibility of its importation into the United States with Australian wheat. Even though it should be imported, however, there would probably not be good reason for excluding the wheat, for the disease in man is usually not serious, and yields readily to treatment. It is much more amenable to treatment than the human favus of the scalp. In mice, however, the disease frequently, perhaps generally, proves fatal.

Samples of Australian wheat from two sources were examined by Buchanan. One sample contained parts of the dried skins of two mice. The latter were so dried, dusty and adherent to the cotton in which they were wrapped that a satisfactory examination proved difficult. No typical favic scutula or crusts were present. Scrapings from the denuded areas showed fungus hyphae, but the material was too meager and in too poor condition to permit a reliable diagnosis. It is possible that the mice examined had been infected, but there was no microscopic proof. Many attempts were made to infect mice and guinea-pigs from these skins and from the wheat. All were without result. No fungus resembling that of favus was secured as the result of numerous culture attempts. If present originally, in the wheat samples or the mouse skins, the fungus probably had died as a result of the prolonged dessication.

In view of these negative experimental results, the question may arise as to the possibility of spores or hyphae of the mouse favus surviving transportation. Data on the longevity of the fungi of this group are not abundant. Sabouraud states that the fungus of favus, at least as it exists in the scutula, remains viable for a considerable period. Sabrazes found that the spores in the scutulum were still alive after two years. Apparently they are more resistant than are those of other dermatophytes. It is not improbable, therefore, that under certain conditions there may be an occasional appearance of mouse favus or, better, of favus herpeticus, among individuals handling Australian wheat in the United States. The possibility of the spores being present in flour and causing infection in bakers is very

remote. Careful studies of the thermal death point of the spores of this fungus apparently have not been made, but related trichophytes have been shown to be readily destroyed by heat. It is not at all improbable, however, that some of the mill by-products used as animal feed may contain viable spores and infect mice, or possibly other animals or man occasionally.

Favus of the Scrotum. A case of favus on the scrotum in a young man of 15, living in Paris, is reported by Gastinel and Pellier.⁶ The lesions had existed for a period of one month and presented the typical godets. The scalp was free, but on the internal surface of both thighs there were circinate, scaling lesions. Examination of the squams disclosed the presence of the achorion.

Localization on Flat Surfaces of Epidermophyton Inguinale. It has long been recognized that *Epidermophyton inguinale* tends to localize in folds of the skin. The most common folds are the interdigital surfaces of the feet, the inguinal region and axillary fossae in order of frequency. It is now becoming recognized, however, that the organism may flourish on flat surfaces and may be found on any part of the body.

Pautrier⁷ has carefully studied two cases and published some excellent photographs of lesions on the legs from which he was able to grow the organism in typical cultures. Sabouraud has stated that when these lesions do occur on flat surfaces they are, as a rule, of short duration and disappear spontaneously. In the two cases observed by Pautrier, the lesions were extensive and the desquamation unusually abundant. In these two cases the infection had its origin in the inguinal folds.

[We have frequently observed areas of epidermophyton infection on the trunk and on the extremities at some distance from the folds where the infection originated. One patient was practically covered with an eruption in the scales of which the organism was abundant. The paper of Charles J. White abstracted on page 60 is of interest in this connection.—M.]

(6) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 3 and 4.

(7) Ann. de dermat. et de syph., September, 1919.

Clinical Study of Epidermophyton Infection. Epidermophyton infection may cause widespread lesions on the flat surfaces of the body which go unrecognized in many cases, even by careful and well-trained observers. The excellent paper by C. F. White⁸ on this subject is of interest in connection with the paper of Pautrier abstracted above. The organism is capable of infecting singly the thighs and adjacent skin, the toes and feet, the fingers and hands, the axillae, the bends of the elbows and of the knees, the flat surfaces of the trunk and extremities and the scalp, or conjointly any combination of the above regions. The clinical appearance of the lesions in the various regions is described in great detail. The type which is of most interest, however, is that affecting the larger flat surfaces of the trunk and extremities. Here the eruption may be eczematiform, psoriasiform, pityriasiform or lichenoid. This last type comes only on apposed surfaces and usually occurs in infections of the upper thighs.

The eczematiform and psoriasiform varieties begin as macules, delicately raised and infiltrated, which soon present a slightly depressed center covered by finely homogenous, yellowish-white, extremely adherent scales. The progress and the extension of these original lesions may be extraordinarily slow. Neighboring areas may not coalesce for weeks, and may even fade away entirely without ever joining each other. As time goes on the primary eruption differentiates into the eczematiform or psoriasiform subvarieties and further description becomes unnecessary, in consequence, except to state that comparatively large surfaces may be covered by direct extensions from the original site. Simulation of eczema seborrheicum may be extreme and an objective differential diagnosis becomes a practical impossibility. It is necessary to say that all these lesions of whatever type remain superficial and always dry unless over-stimulated artificially or secondarily infected, as was once observed in a very fat woman where the disease under one breast and on the upper abdomen took on a multiple impetiginous aspect. When of good size the areas al-

(8) Jour. Cutan. Dis., August, 1919.

ways disappear by central involution, thus leaving curious circles or segments of circles or ellipses. The color is apt to be brick red. Itching or burning may be a striking feature. Resistance to remedies usually successful in combating eczema, eczema seborrheicum, or psoriasis is the absolute rule. When neglected and untreated the disease usually lasts well into the cold weather and then gradually disappears without medical assistance. With the advent of early summer the eruption is apt to recur.

The pityriasiform variety is decidedly rare and presents itself as multiple, homogenously round, fairly sharply defined, delicately furfuraceous, brown-red macules, which resemble in some respects the early lesions of pityriasis rosea and to a greater extent those of tinea versicolor.

One case of infection of the scalp has been observed by White and, so far as he knows, it has never been recorded by any other writer.

The patient was a Jewish cloth cutter, aged 47, who had developed the disease on the left thigh two years previously. One year later the man noticed one pea-sized spot in the frontal scalp, and went to a barber for advice. When first seen by the author, there was a typical epidermophyton infection of the left thigh and contiguous surface of the scrotum and of the perineum and peri-anal region. The man before the present infection had lost most of the hair from the top of his head, but the remaining hairs had persisted. For the most part the follicles appeared as patulous mouths, like the opening of a fine pepper box. In between many of these orifices and covering and obliterating others was a curious, brick-red, rather glistening and seemingly fibrous, curiously tortuous, elevated tissue with no suggestion of scales. Here and there, apart from this extraordinary development, was noted a papery exfoliation somewhat like that of a partly extinguished favus. Owing to technical difficulties, the observations of the writer are not substantiated by microscopic and cultural proof.

Dysidrosis: Its Parasitic Nature. In 1916 Ormsby and Mitchell⁹ published the results of their work on

(9) Practical Medicine Series, 1916, Vol. IX., p. 65.

epidermomycotic infections of the hands and feet. The group of cases forming the basis of the report consisted of sixty-five patients with infections either of the hands or feet or both. The diagnosis of "dysidrosis" had previously been made by trained observers in twelve of the sixty-five cases. In all the cases the organism was found microscopically and in seventeen the organism was artificially cultivated. At that time the finding of the organism in clinically typical cases of dysidrosis was pointed out.

J. Darier¹ is now of the opinion that all cases of dysidrosis will be found to be due either to the fungus infection mentioned above or to a professional or trade irritation.

Darier divides the types into (a) vesicular and bullous (b) vesiculo-squamous and (c) squamous. The three types, mentioned separately in order to emphasize the various aspects which were met with, are evidently only stages in the evolution of the same eruption, but these stages can co-exist at various points of the same extremity. Furthermore, it seems certain that every desquamation does not necessarily follow on a visible vesicular process, and that the affection can persist and progress in the form of dry desquamation.

Is this dermatosis really T. Fox's dysidrosis, or Hutchinson's pompholyx? Is there not amongst these dysidrosiform or eczematoïd eruptions a certain number of cases of epidermic mycoses, and especially of epidermophytosis?

In order to find out, he has submitted the roofs of the vesicles or the squamæ of these dysidrosiform eruptions on hands and feet to microscopic examination as often as possible. Besides negative cases he found positive ones, exactly identical with the others, in which he found, either easily or sometimes with great difficulty, a mycelium.

All the examinations were made by Darier or under his control in his own laboratory. When the first attempt proved negative he adopted the following method: The shreds of epidermis were fixed and the fat removed

(1) Lancet, Sept. 27, 1919.

in alcohol-ether, then separated with needles in acetic acid, finally cleared on the slide in 40 per cent. caustic potash with gentle heat. It was sometimes necessary for success to make several examinations at an interval of some days and to spend several hours in examining the preparations. He has records of twenty patients, three-quarters of whom presented themselves during June, July, and August. In five, all four extremities were affected, nine had dysidrosiform lesions of the hands, and six dysidrosiform lesions of the feet. The total positive results were from eleven to fourteen for hands and from six to eleven for feet. He draws attention to the fact that negative results became more and more rare in proportion as he employed improved technique and greater patience in his investigations. Recently they have only had positive cases, one of which required altogether four hours of work. He believes today that T. Fox's dysidrosis does not exist as a distinct cutaneous disease with a nosologic individuality and that the clinical picture portrayed with great perfection by Fox and Hutchinson corresponds to a parasitic dermatosis—epidermophytosis of the extremities. It will be necessary, however, for further investigations to confirm or upset this conclusion, which at present goes beyond the range of the facts observed by Darier. It will also be necessary to make sure by cultural methods which is the parasite in question and whether it always belongs to one and the same species or not. The morphologic aspect of the mycelium in the squamæ does not allow of settling the question. Sabouraud, consulted on this point, said that he could not say whether it is the mycelium of an epidermophyton that is in question or some species of trichophyton, which alone would certainly be the case if we are in presence of a mycosis of the epidermis.

Darier points out how the hypothesis set up by him as to the probably constantly mycotic nature of the so-called dysidroses fits in with the clinical facts and, on the other hand, with the classic data of dysidrosis and epidermophytosis. It is said that attacks of dysidrosis usually last for from ten to twenty days and often recur in the same subject. This is true of epidermophytosis of the extremities, but it must be added that one

also sees continuous or subintractant attacks prolonged for six months or more. He has seen soldiers who have been made useless for more than half the war by parasitic dysidrosis. Of the etiologic conditions to which dysidrosis is attributed, those which relate to the nervous state, overwork, or dyspepsia are too banal to be considered. The influence of the seasons and the effect of profuse perspiration might consist in the fact that they favor parasitic vegetation. As for the topographic distribution of the lesions, epidermophytosis, like dysidrosis, attacks hands, feet, or all four extremities symmetrically at the same time. Epidermophytosis has, in addition, a favorite seat in the interdigital spaces of the toes, where it is very common; it may persist there for very many years, causing only slight annoyance or even without the patient being at all aware of its existence; thence it proceeds to invade the rest of the feet and doubtlessly the hands also by autocontagion, thus producing dysidrosiform attacks under the influence of occasional causes.

Lesions of the nails have not been noticed in dysidrosis, nor has Darier observed them either in epidermophytosis of the hands and feet, save as chance coincidence. But, on the contrary, it is noticed that the nails are very commonly affected in eczemas and professional dermatites of the extremities. It follows that the good or bad state of the nails can serve as a retrospective diagnosis of a dysidrosiform attack which would be healed at the time of seeing the patient.

Eczematoid Epidermomycosis due to *Saccharomyces*. In 1914 Gougerot and Gaucéa described a case of epidermomycoses of the feet due to a yeast. Since that time Hudelo, Sartory and Montlaur² have observed forty-three cases from which this organism has been grown. The lesion occurred on the interdigital surfaces of the feet as a rule, but also occasionally occurred on the hands. They were likewise encountered in the inguino-crural folds and in the peri-anal region. Clinically, the lesions were characterized by a soft, thick, creamy white, moist epidermis which could be readily detached in large squames. Marked itching was a constant symptom.

(2) Bull. de l'acad. de méd., Nov. 15, 1918.

Microscopically, the cultured cells were found to be of variable dimension and shape; some were spherical whereas others were ovoid or oval. The protoplasm contained large refractive granules grouped about a central vacuole. A few of the cells were budding at both poles but as a rule the budding occurred at only one pole. One type of very large cell occurred in which there was a double-contoured membrane with a peripheral hyalin zone. These cells were budding freely.

Carrot proved to be the best culture medium. Grown on this medium the colonies were of a creamy white color, of smooth contour, with a central mammelated elevation. After the sixth day the color resembled that of *café au lait*.

The organism secretes invertine and produces alcoholic fermentation. It is without action on maltose, galactose and levulose. It liquifys neither gelatine nor coagulated serum. Milk is coagulated. Casein is precipitated and peptonized completely in twenty days.

The yeast was non-pathogenic subcutaneously and intraperitoneally for the guinea-pig and rabbit. When inoculated into an incision on the tongue of a guinea-pig it produced a small tumor from which the organism was recovered. The serum of the inoculated animal agglutinated the emulsified cells at 1 to 100 dilution.

A Case of Tokelau (*Tinea Imbricata*). A case of *tinea imbricata* which occurred in a native of Indo-China who had been in France for two years was observed by Dubreuilh.⁴ The patient stated that his mother and father suffered from the same condition. The patient was covered with large plaques, sharply demarcated, occupying the head, limited at the neck, on the arms and shoulders and in the region of the scapulae, the hands, and forearms, buttocks, legs and feet. There was a marked uniformity of all the plaques. They were sharply delimited and irregularly lobulated, with a small collarette of desquamation. There was complete absence of erythema and infiltration and no tendency toward central clearing. The face presented a reddish color and the desquamation of the hands was more ir-

(4) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

regular and more abundant and the squams were thicker and had a more brownish cast than that of the trunk. The palmar surfaces of the hands and fingers were covered with farinaceous desquamation.

Microscopic examination disclosed a great number of fungi. The patient was treated intensively with all of the accepted local applications for parasitic dermatoses without effect.

Sporotrichosis of the Hand Resembling Trychophyton Kerion. A case of sporotrichosis of the dorsum of the hand which resembled trychophyton kerion so strongly that the diagnosis was impossible until cultures had been made is reported by Maréchal.⁵ The patient was a man 43 years of age, a farmer, who traumatized his hand while on furlough from the army. The traumatism resulted from an injury received while caring for his cow. The development of the lesion had been very rapid and in the course of four months it had attained a diameter of 7 cm. Treatment with potassium iodide was followed by prompt healing.

VITILIGO.

Vitiligo and Syphilis. In a paper read before the Section on Dermatology of the American Medical Association in June, 1919, Lane⁶ has attempted to collect the case reports in which the question of the relationship of syphilis and vitiligo is discussed, and has examined most of the literature on the achromias and dyschromias published since 1906. That date is a convenient starting point, because it was the year of the publication of the discovery of the Wassermann reaction. It has, however, been impossible to consult much of the German literature of the last few years.

In a total of 118 cases of vitiligo, sixty-one or 51.7 per cent. were demonstrated to be syphilitic; nineteen, or 16.1 per cent. were hereditary syphilis; fifteen or 12.7 per cent. had suggestive, though not characteristic, signs of hereditary syphilis; forty-two, or 36.5 per cent. were

(5) *Ann. de dermat. et de syph.*, September, 1919.

(6) *Jour. Amer. Med. Ass'n.*, July 5, 1919.

negative, or if the suspicious but unproved cases, be included, fifty-seven or 48.3 per cent. were negative.

There are, however, certain evident characteristics of statistics of this sort which prevent them from being taken at their face value. The chief one is that they are composed for large part of reports of one or two cases by different observers, many of whom have reported positive cases, only, perhaps having been interested in the subject for a short time and having chanced on a case or two in which syphilis was evident. Such statistics inevitably give an unwarrantedly high percentage of positive cases. The statistics are likely to be of more value when a considerable number of cases have been carefully studied by one observer. Among the reports received by Lane, those of Joltrain, Vignolo-Lutati, and Withe and his associates are of especial interest.

Joltrain examined eighteen patients with vitiligo of whom thirteen or 72.2 per cent. were syphilitic; three or 16.6 per cent. hereditary and five or 27.8 per cent. were negative. The details of the examinations made by Joltrain are not given but they were undoubtedly thorough, though examination of the spinal fluid was probably not made in the negative cases.

Vignolo-Lutati examined fifteen patients of whom five or 33.3 per cent. were syphilitic; three or 20 per cent. hereditary and ten or 66.7 per cent. were negative. The reports of positive cases showed careful investigation of the patients and though nothing is said in regard to those found not syphilitic, it is to be presumed that these were examined with the same care. Here again it is probable that the spinal fluid was not examined in the cases that were otherwise negative.

The report of Withe and his associates is of the greatest value and deserves closer examination. The patients on whom the report was based were studied at the weekly meetings of a group of English, French and Belgian army officers during the war. All but two of the patients were soldiers, and these two were women. The opportunities for study of the patients were ideal, as all necessary examinations could be made. The pa-

tients were all carefully examined, spinal fluid examinations and provocative injections of arsphenamin were made in doubtful cases, thereby revealing three positive cases that would otherwise have remained negative or unproved.

Fifty patients were examined, of whom fourteen or 28 per cent. were syphilitic; five, or 10 per cent. were hereditary; fifteen, or 30 per cent. showed signs, suggestive but not conclusive, of hereditary syphilis; twenty-one, or 42 per cent. were negative; or counting the suspicious but unproved cases as negative, thirty-six, or 72 per cent., were negative.

The results obtained by these three observers show a striking similarity. Taken together, they give the results shown in the accompanying table, all unproved cases being classed as negative.

RELATION OF VITILIGO TO SYPHILIS IN THE CASES OF THREE OBSERVERS

	Number of Patients	Syphilitic No. Per Cent.	Hereditary No. Per Cent.	Negative No. Per Cent.
Joltrain	18	13 72.2	3 16.6	5 27.8
Vignolo-Lutati	15	5 33.3	3 20.0	10 66.7
Withe et al....	50	14 28.0	5 10.0	36 72.0
Total	83	32 38.5	11 13.2	51 61.5

Of eighty-three cases of vitiligo thirty-two or 38.5 per cent. were in syphilitics. Not included in the figures given in the table there were in Withe's series four additional patients who had vitiligo previous to contracting syphilis. These observations confirm those made previously by Thibierge, though their deduction differs from his. They conclude that "this fact is not an objection to a primary hereditary infection. Binary syphilis must be especially frequent in the attenuated forms of hereditary syphilis."

Discussing the fifteen patients who showed signs suggestive of hereditary syphilis, but in whom syphilis could not be certainly demonstrated, Withe and his associates say that "if vitiligo begins in infancy, it frequently coexists with signs which may be interpreted as

belonging to a benign form of hereditary syphilis; on the other hand, the classical signs of hereditary syphilis are lacking in such cases." The deduction made by them from their results is that "it is impossible to arrive at the definite conclusion that there is a relation of cause and effect between syphilis and vitiligo, but the intensive study of the case (including reactivation) is causing this hypothesis to gain ground."

Vitiligo with a Central Mole. Two cases of vitiligo having moles in the center of the vitiliginous patches are reported by J. L. Bunch.⁷ The author refers to these as being "almost unique." The first patient was a girl 12 years old who had the hair removed by Roentgen rays six years prior to coming under observation, because of ringworm of the scalp. The hair grew in again and was normally pigmented. For about a year she had two well-marked patches of canities which had remained unchanged. Simultaneously there developed patches of vitiligo which numbered thirty-five in all, and which varied in size from a five-shilling piece to a sixpence (approximately from a dollar to a dime). In the center of several of these was a raised, pigmented lesion resembling a mole. One of these patches was on the neck and the other on the body.

The other case occurred in a girl 9 years of age who had been under observation for two years. She had several patches about the size of a five shilling piece on the trunk, one of which had a well-marked central brownish-black mole-like lesion. Histologically, the horny layer was found somewhat thickened. The rete mucosum was not thickened but sent down-growths into the corium. Throughout the growth, which was localized, were masses of cells in the upper part of the skin a definite arrangement in petals containing pigment. In the lower part there was no definite arrangement, but the cells were scattered irregularly among the connective tissue cells of the corium.

[A case of vitiligo with a central mole was shown by Dr. Hyde before the Chicago Dermatological Society and a description of the case appears in the *Journal of Cutaneous Diseases*, 1906, p. 84. The patient was an

(7) Brit. Jour. Dermat., October-December, 1918.

Italian, 25 years of age, who had had the disease for four years. He had sought relief for syphilis and in the course of the examination the vitiliginous lesions were discovered. There were present on his body twelve circular vitiliginous areas varying in size from a split-pea to that of a silver half dollar, in the center of each of which was a reddish papule. The papule often surrounded a hair follicle, and bore a definite relation in size to the area of vitiligo in which it was situated.

In the course of the routine examination of troops for discharge at Camp Funston and Camp Pike six cases of similar vitiligo were observed. All the lesions were on the trunk and usually about the level of the waist, either in the lumbar or flank regions. Inasmuch as the lesions gave the patients no trouble it is not to be expected that they would consult a physician because of the condition.

We have recently seen a patient who had a typical lesion over the right deltoid. The man had presented himself for treatment for another condition and this lesion was discovered in the course of the routine examination.—M.]

ALOPECIA.

Generalized Alopecia of Suprarenal Origin. A case of generalized alopecia which came to autopsy was studied by Balzar and Barthélémy.⁸ A generalized alopecia has been frequently attributed to thyroid insufficiency because of the existence of Graves' disease or to other evidences of hyperthyroidism in patients manifesting alopecia of the areata type. Cases of generalized alopecia of suprarenal origin, however, are much more rare. It is well known that suprarenal disturbance may influence the nutrition of the teeth and hair, particularly that of the pubic region. The patient was a man 39 years old who had syphilis and pulmonary tuberculosis. The immediate cause of death was tuberculous pneumonia and the remote cause was a marked Potts' disease. The kidneys were found to be filled with

(8) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6

small tubercles, the suprarenal capsules were enormously augmented in volume, very hard, lardaceous, white, and in the right a large cavity was found. The thyroid was somewhat below normal size and indurated. The hypophysis was apparently normal.

Post-Influenzal Alopecia. A study of twenty-four cases of post-influenzal alopecia by Samuel Ayers⁹ shows that the alopecia occurs commonly about two or three months after the onset of the influenza, but occasionally during convalescence. The alopecia is usually of the diffuse type, although in one of the hospital cases and one private case the lesions were patchy and, without a history of influenza, might have been diagnosed alopecia areata. Twenty-one of the twenty-five consecutive cases were in females and all of the twenty-five patients were under thirty-six years of age.

Alopecia following any severe febrile affection is a common occurrence. There is still some question as to whether the loss of hair after fevers is due to interference with the nutrition or to a toxin acting directly on the hair papillae, although the former view is more generally held. Most of the writers agree that a pre-existing seborrhea makes the loss of hair more certain.

H. H. Hazen¹ reports the observation of fifty patients suffering from alopecia following influenza. Of these, three were men and forty-seven were women. It is highly probable that women are more inclined to consult a physician because men feel that the affection is trivial and hardly worth troubling about. As the epidemic was more severe among the young it is only natural that the alopecia patients were all young. Unquestionable, the severity of the disease has much to do with the subsequent loss of hair. One-third of the patients had had severe pneumonia, and only five of the fifty had had fever of less than 102.5° F. It is doubtful if a pre-existing seborrhea played any great part for twenty of the fifty stated that they had had practically no dandruff and the scalps of twenty-two of the fifty were absolutely free from any local trouble. The average beginning of the alopecia was nine weeks. The shortest

(9) Boston Med. and Surg. Jour., April 24, 1919.

(1) Jour. Amer. Med. Ass'n., May 17, 1919.

time elapsing from the onset of the influenza to the time was two weeks, and the longest three months. The amount of hair lost varied greatly. In one case there remained only one tuft of hair on the back of the scalp and as another extreme, not more than a tenth of the hair was lost. As nearly as could be estimated largely from the thickness of braids, the average loss of hair was from one-third to one-half. As a rule only the long hairs fell, and these were almost immediately replaced by short hairs, so it is probable that new hairs simply push out the old hairs that have been damaged. The greatest loss of hair was usually over the anterior and parietal portions of the scalp. The alopecia was diffuse, not patchy, although in two cases there was a tendency toward patchiness. In one instance there was one completely bald area about $1\frac{1}{2}$ inches in diameter. Only twelve of the patients complained of sensitiveness, either local or general, of the scalp. In the forty-one cases both scalp and hair were abnormally dry.

Post-influenzal alopecia differs in no wise from any other postfebrile alopecia. In practically all cases the prognosis is excellent. Simple cleansing of the scalp and a stimulating tonic with ordinary hygiene of the scalp is all the treatment required.

Loss of Hair due to Lightning. During a thunderstorm in October, 1918, according to T. Ashby,² a house was struck by lightning and much damage done. Three children, a girl of 9 years and two boys, aged 7 and 5 years, were in the same bed on the first floor. According to the mother's statement the children were all lying with their heads up at the same end of the bed, and all were asleep on their right side, as was their usual custom. The children were naturally frightened by the thunder and lightning, but did not suffer any harm. A fortnight afterward the hair on the left side of their heads from the middle line downward began to come out, and in a few days the scalp on the left side was quite denuded of hair. The right side of their heads was protected from the lightning by the pillow. Three months later, the hair was slowly growing again, and all the children were in good health. The lightning seems

(2) Brit. Med. Jour., March 15, 1919.

PLATE III.



Acute type of lichen planus.—Fordyce and MacKee, page 78.

PLATE IV.



Lichen planus of the palms.—Fordyce and MacKee, page 78.

PLATE V.



Lichen planus of the soles.—Fordyce and MacKee, page 78.

PLATE VI.



Lichen planus of the lips.



Lichen planus of the tongue.



Lichen planus of the glans penis.
—Fordyce and MacKee, page 78.

PLATE VII.



Lichen papules in scratch marks.



Linear hypertrophic lichen planus.—Fordyce and MacKee, page 78.

PLATE VIII.



Lichen planus linearis.—Fordyce and MacKee, page 78.

PLATE IX.



Lichen planus papules showing umbilication.—Fordyce and MacKee,
page 78.

PLATE X.



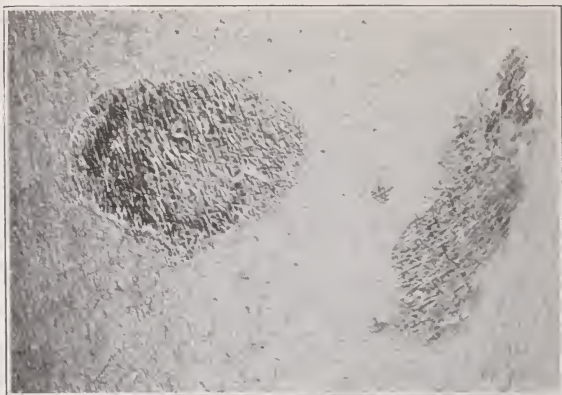
Lichen planus annularis.—Fordyce and MacKee, page 78.

PLATE XI.



Lichen planus annularis with pigmentation.—Fordyce and MacKee, page 78.

PLATE XII.



Lichen planus annularis with pigmentation and rolled edge.



Lichen planus hypertrophicus with pedunculated tumor containing large follicular plug.—Fordyce and MacKee, page 78.

PLATE XIII.



Lichen planus resembling psoriasis and chrysarobin staining.—Fordyce and MacKee, page 78.

PLATE XIV.



Lichen planus suggesting syphilis.—Fordyce and MacKee, page 78.

to have had a direct effect on the hair follicles like the x-rays.

Frequency of Seborrhea and Absence of Alopecia in Algiers. Seborrhea of the scalp has long been recognized as a cause of alopecia of the vertex. It has been maintained by some writers that seborrhea in the Musulman is non-existent or extremely rare. Montpellier² has made a careful study of the scalps of Algerian natives and has found that seborrhea of the scalp is quite as frequently encountered as it is among the Europeans. The natives are very little concerned about cleanliness, and, moreover, they wear the heavy head dress peculiar to the Algerians and if, as we are inclined to believe, seborrhea and hats are a cause of baldness, one should encounter alopecia very frequently among the Algerians. Baldness, however, is extremely rare among the natives.

LICHEN PLANUS.

Lichen Planus. At the Annual Meeting of the American Dermatological Association at Atlantic City, in June, 1919, Dr. E. Graham Little,⁴ of London, was the guest of the association and opened the symposium on lichen planus with a paper. This paper was the result of an intensive study of 270 cases and is the most comprehensive and valuable contribution to the subject of lichen planus of recent years.

Little is quite in sympathy with the French suggestion that we should discard all other names and speak simply of lichen of Wilson. The adoption of this terminology would spare us the incongruity of writing such inconsistent titles as "lichen planus acuminatus," "lichen planus verrucosum," which are obviously contradictions in terms. Moreover, lichen scrofulosorum and lichen ruber should be eliminated because of the confusion which results, inasmuch as neither disease has anything to do with lichen of Wilson.

Of the 270 cases, 171 were in females and ninety-nine

(3) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(4) Jour. Cutan. Dis., October, 1919.

in males. Before the war the ratio of men to women was 6 to 11; after the beginning of the war the ratio was changed to 4 to 11. The difference is, in all probability, explained by the circumstance that the male patients decreased materially with the progress of war and the conscription of adult males rather than that the ratio was altered for any other reason.

The age incidence was found to range from 5 to 85 years, with an average age between 35 to 55, a period which covers the climacteric in women. There was an acute onset in an unusual proportion of the cases; this was particularly true in the linear cases. In a few instances there were general illness and arthritic pain. In one case bullae were found in some of the lesions.

The three types of initial lesions, the plane papule, the acuminate papule and the white papule are described in great detail, both macroscopically and microscopically. The author is of the opinion that the burnished surface of the papule, or the mother-of-pearl sheen, has been unduly stressed as being of special diagnostic import. This feature is closely simulated by the lesions of papular urticaria in children and led so acute an observer as Colcott Fox to class this latter affection as "lichen infantum," a classification which he entirely repudiated in after life. Little also is of the opinion that the striae described by Wickham are infrequently present and seldom offer any real aid in diagnosis.

The occurrence of the acuminate papule is rare and in the absence of the plane papule would certainly cause much difficulty in reaching a diagnosis because of the close similarity with the papule of pityriasis rubra pilaris. He is quite in accord with the observations of Ormsby concerning the white papule of lichen sclerosus, although he has seen but one case, whereas Ormsby in his original paper described six cases.

Histologically, round-cell infiltration is found around the vessels of the papillary body, which as a result is much enlarged. The character of the cellular infiltration is much discussed and there is little agreement as to the nature of the cell. Most writers agree that the epidermis is thickened, the stratum corneum and the granular layers being hypertrophied, especially the lat-

ter. The eleidin is irregularly deposited, and usually three or four layers of eleidin-charged cells may be made out. This is one of the most important features of the histology and is common to all varieties of true lichen of Wilson. The acuminate papule has a distinct histology from that of the plane papule. It centers around a hair follicle and there is, consequently, a strong superficial resemblance to the papule of pityriasis rubra pilaris, from which it is distinguished, according to Unna, by the presence of edema, colloid degeneration of the epithelium, hyalin degeneration of the blood-vessels and the fibrosis of the connective tissue.

The distribution of the plane papules is singularly constant in certain sites, of which the front of the ears, the inner side of the knee, and the nape of the neck are perhaps the commonest. Next in frequency are the sacral region, the upper and anterior aspect of the thighs, the chest and flexor of the elbows and the lower abdomen. On the mucous membranes, the tongue is less frequently diseased than the mouth, and the lip least of all. The mucous membrane of the cheeks is probably the most common of the mucous surfaces to be affected. Of the 720 cases there were forty-eight in which mouth lesions occurred.

On the glans penis two forms of eruption may occur, either the white ridges as in the cheek along the interdental line or, more commonly, the red papules arranged in ring shapes.

Of the clinical varieties, the author found the linearis and the annularis fairly frequent, whereas the moniliformis is extremely rare. There were thirteen cases of the linearis type, of which five occurred in children under twelve years. One interesting feature of the linearis type is the remarkable rapidity with which a solid line of papules three feet in length may be built up. In one case a line from the buttock to the heel developed in six weeks. As a rule, the linear type is asymmetrical and very intractable to treatment.

Concerning the formation of the lichen planus annularis type of lesion there has been some controversy as to whether the ring results from a circinate juxtaposition of individual papules, or whether from an involu-

tion of a large papule or patch which clears in the center while remaining active at the periphery. In the author's series there occurred twenty-two cases of the annularis type, and therefore it comes next in frequency of the special types to lichen planus hypertrophicus.

Lichen planus hypertrophicus or verrucosus occurred in forty cases, and is therefore the most common of the special varieties. The initial lesion has usually been thought to be acuminate, but the hypertrophic type is quite common in association with ordinary planus eruptions. The persistence of hypertrophic lesions is much greater than that of any other type and the warty growth may attain a huge size. The lesions are usually unilateral and they are far more frequently found on the lower than on the upper parts of the body.

The occurrence of lichen spinulosus and lichen planus in the same patient was first observed by MacLeod and Dore. This is interesting inasmuch as Little was the first to describe the occurrence of lichen spinulosus with folliculitis decalvans in the same patient. He is of the opinion that lichen spinulosus is not a phase of lichen planus and that there is no connection between the two diseases.

The etiology of the disorder is discussed by Little at some length. A test of the nervous theory so long held by many men was afforded by a study of the statistics of the frequency of the occurrence of the disease before and after the war. The author's statistics compared with those of Crocker show that in the period between 1909 and 1918 lichen planus was only one-half as frequent as in the earlier period of Crocker. Thus Crocker in 10,000 cases prior to 1893 saw ninety-eight cases of lichen planus, an incidence of 1 per cent. In 30,000 cases of skin diseases seen at St. Mary's Hospital, Little observed lichen planus in 150, an incidence of 0.5 per cent. Adamson, Lancashire, Norman Walker, Dore, MacLeod and Skinner all furnish data showing a positive diminution in cases after 1914 as compared with equal periods before that date. The incidence of lichen planus among the British troops is very difficult to estimate for the reason that expert diagnosis was rarely

obtainable. In one valuable personal experience of this kind, that of MacCormac, who was in charge of the big base hospital for skin diseases, lichen planus seems to have been extremely rare. If the civil population endured the nervous exhaustion of suspense and privation the army must have had a plentiful experience of shock, and yet no corresponding increase of lichen planus is reported in army or civil population during this period.

Little does not believe that focal dental sepsis can be a factor in the etiology of lichen planus, inasmuch as carious teeth are very common in the civil and military population of Great Britain. Whatever the cause of lichen planus may be, its proportion is declining.

The treatment found by Little to be of most value consists in intramuscular injections of 2 c.c. of enesol, a combination of arsenic and mercury prepared in France. As a rule, the disorder will yield to these injections within six weeks.

[During the period between December, 1918, and June, 1919, thousands of men were examined prior to discharge at Camp Funston. If shock were a factor in the etiology of lichen planus one would suppose that this disorder would be frequently observed among combat troops returning from overseas. During this period, however, not a single case of lichen planus was seen.—M.]

Lichen Planus in Private Practice. After an intensive clinical study of sixty-four cases of lichen planus which he had seen in his private practice, Charles J. White⁵ summarizes the findings as follows:

Lichen planus is a subacute and at times an acute disease. It affects largely the educated classes and especially those whose immediate past has been troubled; rarely it follows an injury. It seems to occur more often in women than in men. It appears largely in the fourth and fifth decades of life. It varies greatly in duration—a few cases come and go in a few weeks; many last months; some may persist even for sixteen years. The initial lesions may favor the flexor surface of the wrists, but they may and do appear on almost any part of the body, and even on the mucous membranes

(5) Jour. Cutan. Dis., October, 1919.

where the characteristic violet coloration becomes silvery white. The eventual distribution of the eruption may be universal. The typical objective lesion is an almost pathognomonic papule, but many variations occur, and occur commonly. The disease is always pruritic, and the entailed suffering is at times almost unbearable. Pathologically, we note an initial change in the corium and a subsequent epidermic alteration. The most characteristic pathologic feature is the almost geometrically straight, inferior border of the cellular infiltration. The infiltrated macroscopic lesions for the most part terminate in chocolate-colored macules. Treatment is palliative. Cure seems to depend largely on natural evolution.

Clinical Types of Lichen Planus. Although lichen planus is not rare in dermatological practice, nevertheless the general practitioner is infrequently consulted by a patient for this disorder. The various clinical types of lichen planus are described in detail in an instructive article by Fordyce and MacKee.⁶ The illustrations accompanying this article are of such excellence that as many as possible are herewith reproduced (Plates III to XIV).

Lichen Planus in Two Brothers. Lichen planus is a rare disorder and the occurrence of two cases in one family is a coincidence worthy of note. Montgomery and Culver⁷ observed two brothers, one of whom was 40 and the other 30 years of age, with lichen planus. The disease appeared first in the elder brother, ran a characteristic course and finally yielded to treatment. About two years later, the younger brother presented himself for treatment. The older brother was a rancher, and the younger a druggist. They lived in widely separated communities. Both men were found to have marked disturbances of the gastro-intestinal tract.

Lichen Acuminatus. An intensive study of the literature and a careful clinical study of a case lead S. Feldman⁸ to the conclusion that pityriasis rubra pilaris and lichen acuminatus are identical diseases. In the

(6) Jour. Cutan. Dis., May, 1919.

(7) Ibid, April, 1919.

(8) Ibid, April, 1919.

author's case, the onset was preceded by an erythema. The lesions first appeared on the backs of the first and second phalanges and the disease ran a benign course. There was no sign of a hair structure in the corneous plug. The presence of the eruption in the mouth links it closely with lichen planus.

Lichen Planus et Acuminatus. An interesting case presenting both the acuminate and the plane papules of lichen of Wilson is reported by Fernet and Scheikevitch.⁹ The patient was a woman 23 years old who first entered the service of Brocq for an extensive ulceration of the heel and plantar surface of the left foot. Lesions of the tongue, areas of alopecia and diffuse pigmentation of the extremities and of the trunk were present. The lesions first appeared on the feet and later on the tongue. This led to a diagnosis of hereditary syphilis and in spite of several negative Bordet-Wassermann reactions arsphenamin injections were instituted, without any appreciable result. The lesions continued to develop, when suddenly typical lichen planus papules, together with the acuminate papules appeared. Later an examination of the lesions of the trunk and the internal surface of the cheeks showed typical white, linear lesions of lichen planus of the mucous membrane. A biopsy of the cutaneous papules confirmed the clinical diagnosis.

HYPERKERATOSES.

Porokeratosis. A case of porokeratosis, which is remarkable because of its extent, is reported by MacCormac and Pellier.¹ The patient was a man, 27 years old, who, prior to his four years of military service, had been employed in chemical work, and while there had sustained a burn with sulphuric acid. The disease began about the middle of the hand, spreading thence down to the fingers and up the arm and onto the chest and neck. For about one year after the onset it had progressed with some rapidity, after which time further

(9) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(1) Brit. Jour. Dermat. and Syph., October-December, 1918.

extension had been slow or negligible. Weakness of the left hand was also complained of.

When first seen by the authors, the distribution was as follows: Lesions existed on all the fingers and the thumb, extending up the front of the forearm in an irregular band; the left shoulder, left axilla and left side of the neck were also involved. A series of lesions followed a sinuous course over the left breast, turning up from the lower end of the sternum to take a line sharply limited to the middle of the body. Other lesions were clustered together over the left scapula and left shoulder.

Given in greater detail, the disease in the various regions was of the following nature: All the nails of the left hand, except the thumb-nail, were affected, having become thickened, rough, and brittle, and raised from the nail-bed at the free end. On the hand the palmar surface was chiefly involved, the characteristic features of porokeratosis being well developed, *i. e.*, a peripheral rampart, on the summit of which there was in places a fine sulcus containing a tiny horny ridge. The skin enclosed by this rampart was red, slightly scaly, but not atrophic. On the wrist and forearm similar lesions were seen, with, in addition, numerous horny papules with central plug. On the upper arm, shoulder and breast a less advanced stage had been reached: the rampart was ill-formed, the lesions smaller, many of the circles being made up of groups of small conical horny papillae. In the axilla these had become sodden and moist. Two small, slightly elevated, dirty white spots, each larger than a pin-head, were found present on the right side of the dorsal aspect of the tongue.

Histologically, there was hyperkeratosis of the mouth of the sweat-ducts, and this process was also found at the orifice of the hair-follicles. This is in agreement with the recently published observations of Matsumoto.² There was a slight increase in the number of cells in the rete, and this had lost to some degree its characteristic papillary arrangement, presenting a flattened-out

(2) Practical Medicine Series, 1918, Vol. VII., p. 72.

appearance. In the papillary and subpapillary regions moderately dense cell infiltrations existed, and cell infiltrations were also present around the sweat-glands and small blood-vessels.

The original views of Mibelli can not be sustained by the findings indicated above, nor are the early lesions on the tongue, found in this case, in accordance with the theory of a sweat-duct origin. In the illustrations it is seen that the general arrangement bears some resemblance to a unilateral nevus, as in the case reported by Truffi.

Non-Congenital Ichthyotic Erythroderma. True ichthyosis is generally considered to be congenital in all cases. Simple xerosis is sometimes not apparent until the patient has changed climates and gone from a warm to a cold climate. An erythroderma which lay intermediate between pityriasis rubra pilaris and ichthyotic erythroderma is reported by Fernet and Scheikevitch.³ The patient was a man 51 years old who first entered the hospital in 1914 for a weeping, squamous, red dermatosis. After a few days in the hospital he developed generalized erythroderma. At this time he had on the dorsal surface of the hands and about the neck follicular keratotic cones which led to the diagnosis of pityriasis rubra pilaris. It was also found that he had plantar and palmar keratoderma of very marked degree which was more accentuated than usually accompanies pityriasis rubra pilaris. The patient left the hospital and later returned with atrophy and scleroderma of the skin of the extremities. The same plantar and palmar keratoderma had by that time formed large, thick, succulent, cornified masses. The keratoderma of the palms and soles, the lesions on the flexor surfaces, and the seborrheic, squamous changes of the scalp were all characteristic of congenital ichthyotic erythroderma. The atrophy and sclerodactylia was characteristic of neither pityriasis rubra pilaris nor of congenital ichthyosis. Taken as a whole, the appearance of the patient was that of a condition which has been described under the term "*Erythrodermie congénitale ichtyosiforme avec hyperépidermotrophie.*"

(3) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 3

Hereditary Corns on the Palms and Soles. Kaposi was probably the first to report a case of circumscribed hereditary hyperkeratoses on the palms. The case, however, was not studied in detail and little is known about it. Audry⁴ describes in detail a case of hereditary corns on the palms and soles which occurred in a woman 41 years old. The lesions had been noticeable since the fifteenth year. The same lesions existed in her grandfather, her mother, and three maternal aunts. Her three maternal uncles, however, and her own son were free from the disorder. On the palmar surface of the palms and fingers, disseminated in great number, were hyperkeratoses of the size of a sago grain. They were

and 4. imbedded in the epidermis, through which they projected slightly. There was no evidence of inflammatory reaction, and the lesions had the usual hard, corneous center implanted in what appeared to be normal skin. Aside from a slight hyperidrosis, the patient's hands were normal. The corns on the feet were similar, but less elevated and less numerous than those on the palms and were located on the plantar surfaces of the toes.

Plantar and Palmar Punctate Keratoses. Two interesting cases of plantar and palmar punctate keratoses occurring in first cousins who were also man and wife are reported by Galloway and Adamson.⁵

One of the patients was a frail woman 35 years of age who had suffered from the presence of the punctate lesions on her hands and feet since her girlhood. The keratoses were yellowish-brown, flattish nodules which varied in size from minute points to that of millet seeds. The nodules were papules which consisted of very horny epithelium and were never vesicular. In time the nodules tended to flatten, and finally became depressed below the surrounding surface. Many of the papules showed definite pitting at the summits or centers. The patient stated that the nodules had recently increased in number. The condition of the soles was the same as that of the palms.

The papules were painless, and caused the patient no

(4) *Ann. de dermat. et de syph.*, September, 1918.

(5) *Brit. Jour. Dermat. and Syph.*, July-September, 1918.

inconvenience except that when the lesions became long they caught in her needlework. To prevent this she made a practice of trimming or digging out those lesions which became troublesome.

The case of the husband was similar to that of the wife but much less severe.

Histologic examination disclosed nothing of interest. The treatment consisted in the local application of a salicylic acid ointment without much improvement. In the discussion which followed the presentation of these cases before the Dermatological Section of the Royal Society of Medicine, Adamson and Weber were of the opinion that the cases were of the nature of nevi.

Symmetrical Keratoderma. A case of extensive keratoderma in a child 5 years of age is described by Vilvandré⁶ of Sequeira's clinic in London.

The patient had suffered from no illness except measles, and no other member of the family (there were five other children) was affected. The father and mother were also healthy and free from any skin affection. There was no history obtainable of any hereditary factor. The skin of the affected areas was thickened, of greyish-black color, with some hypertrichosis. The hands, forearms and elbows, both feet, part of the legs, especially the knees, were involved. On the lower extremities the lesions, wider in extent at the knees, tapered to a point on the tibiae and the thighs in the form of lozenges. The plantar surfaces of both feet were symmetrically affected, and the lesions were of a dark, blackish-grey color, and deeply fissured, resembling the bark of a tree. The dorsal aspects of the feet were also involved, where the affection extended in a pointed manner to the lower part of the legs. The hands, both dorsal and palmar aspects, were affected, and the indurated, thickened skin reached to the elbows on the anterior aspects, and to just above the wrists on the dorsal surfaces.

The case appears to fall into the group of symmetrical hyperkeratoses, of which tylosis is the more common type. The case differs from common tylosis in the invasion of

(6) Brit. Jour. Dermat. and Syph., October-December, 1918.

the knees and the dorsal surfaces of the adjacent parts of the limbs.

Keratoderma Blennorrhagica. A case of keratoderma blennorrhagica in a man who entered the hospital for an arthritis of the left knee is reported by S. C. Dyke.⁷ He was treated with salicylates from the first of May to the last of June, during which time no one had discovered the presence of the gonococcus urethritis.

About the beginning of July, the condition of the patient's feet began to attract attention. On admission, the skin of the plantar surface was thick and calloused and showed a tendency to come off in crusts. This process is occasionally seen in men after they have been in bed some weeks, and no particular attention was paid to it until it was noticed that as the flakes separated they did not leave clean pink skin underneath; on the contrary, as the flakes of thickened epidermis came away new ones formed underneath them. This condition became rapidly aggravated until the whole plantar surface, the sides of the feet, and the dorsal surfaces of the ungual and, to a less degree, of the second phalanges were covered with a thick horny layer of desquamating epidermis. Cracks appeared in this desquamating layer, which was shed in fragments from the size of half-a-crown to a fine dust. As fast as the epidermis was thrown off further keratization occurred in the underlying epithelium, which was later in its turn desquamated. The process went on underneath the nails, most of which in time separated and came away. Some traces of the same condition, in the shape of a branny desquamation around the finger-nails occurred on the hands. The palms were not affected. No inflammatory reaction accompanied the process, which was almost painless.

A course of gonococcus vaccine was given from July 10 to August 10. A start was made with a dose of 5 millions and the dose was worked up to 300 millions; 850 millions was the amount given in the course of the month. The improvement in the condition of the feet was immediate and marked. After the first few doses, the further keratization beneath the already separating

(7) *Lancet*, Aug. 23, 1919.

epidermis ceased, and at the end of the month most of the thickened skin had separated, leaving normal epidermis beneath. At the same time the pyrexia ceased. The joint condition, which, under radiant heat and massage, was improving before the commencement of the vaccine, showed no marked change.

Arsenical Keratosis. A case of severe keratoderma due to ingestion of arsenic over a long period is reported by W. McMurray and L. P. Johnston⁸ of Sydney. The patient was a man 33 years of age who had had the condition for five years.

The patient stated that he commenced to have "fits" fourteen years ago and had been taking a mixture since that time for the purpose of warding off the attacks. The skull had been trephined but without relief for the seizures. During the past fourteen years, the patient had had many attacks of vomiting and severe diarrhea, no doubt due to the arsenic in the prescription he had been taking.

The patient had well-marked keratoderma of the soles and palms; these thickened areas were covered with punctate keratoses. The body, especially the trunk, showed the well-marked rain-drop pigmentation due to arsenic. The patient also showed the silver tongue of chronic arsenical intoxication.

[All prescriptions for arsenic should be marked "not to be refilled." Patients with dermatitis herpetiformis, psoriasis, lichen planus and various nervous diseases have prescriptions given them containing arsenic. The patients discover the temporary benefit they derive from the drug and they continue to take it. For various reasons they fail to keep themselves under the observation of the physician who prescribed the arsenic. The result is that after a year or more the individuals develop generalized keratoses, a condition which may be worse than the original dermatosis.—M.]

Arsenical Eruptions. While in the dermato-venereal center at Tunis, Jamin⁹ had the opportunity of observing twenty-nine cases of arsenical eruption which arose through an effort on the part of soldiers to avoid

(8) Med. Jour. Australia, Aug. 30, 1919.

(9) Bull. Soc. franc. de dermat. et de syph., 1919, No. 1.

military service. These men had taken a mixture of thapsia roots, honey and arsenic. They were able to get the arsenic from the depilatory preparations much used by Arab women. One dose was enough, according to the patients, to produce the desired effect upon the skin, which appeared on the second day after the ingestion. All the cases commenced in very much the same way: Gastro-intestinal symptoms usually were the first to appear and, as a rule, came on very suddenly. This was followed by an erythema consisting of lentil-sized red areas, rounded and sharply demarcated, and disappearing under pressure. These were usually localized on the extensor surfaces of the four extremities. On the day following the onset the eruption became confluent on the extremities and continued to generalize over the entire cutaneous surface. The aspect then was that of a primary acute erythroderma.

The cases tended to fall into one of two classes: The first was a mild form characterized by lack of fever, absence of albuminuria, an eruption of morbiliform type limited to certain areas and not involving the mucous membrane. This afebrile form usually cleared in about three days, leaving nothing but a furfuraceous desquamation analogous to that of scarlet fever. There was no itching, but following the disappearance of the eruption there was usually some pigmentation.

In the intense form, all the phenomena of the mild form were markedly accentuated and there was profound systemic disturbance. The onset was marked by intense headache, vomiting, diarrhea, and sometimes by epistaxis. The fever reached 40° C. Sometimes the erythema was papular, like an irritated urticaria. Occasionally it was in well-defined plaques, suggesting erysipelas. At other times it had the appearance of multiform erythema. One case had lesions closely suggesting those of pityriasis rosea. In a few cases itching was later rather intense. The eyelids, lobes of the ears and the elbows sometimes showed soft phlyctenules containing a yellow, serous fluid. The mucous membrane in this severe form was frequently involved and showed bullae analogous to those of the skin.

The evolution of this severe form was quite regular.

The temperature which was at first around 40° C. descended by lysis to normal about the sixth day, after which there was a subnormal temperature for several days. The pulse followed the temperature, but it descended more rapidly. Bradycardia was quite marked. There was no hypertension. The pulse was slow, well-marked, vibrant beneath the finger, and of a cerebral type, suggesting a mild bulbar intoxication. As a rule, it increased to normal along with the temperature. During this period some of the patients were observed in profound asthenia not unlike that of typhoid. There was a reduction in the urine and usually albuminuria. After the erythema disappeared the desquamation commenced. It began, as a rule, with small lamellae in the regions of the thickened epidermis and in some cases it came off the hands and feet as gloves and sandals. One patient presented an appearance which was strikingly like that of pemphigus foliaceus. Others suggested very severe and extensive burns. One case was followed by arsenical keratoses about the ankles.

The author was unable to determine the rôle played by the thapsia in the production of the dermatitis. One of his colleagues in Tunis said that it was possible to produce similar eruptions by the use of thapsia alone.

PEMPHIGUS.

A Clinical Study of Pemphigus. During the past five years, Goldenberg and Highman¹ have had the opportunity to study thirty cases of pemphigus in the wards of Mt. Sinai Hospital. No special investigations were made directed toward a solution of the etiology of the disease, but the clinical facts have been correlated in the hope that some light might be shed upon some phase of the fatal dermatosis.

A study of the cases has led the authors to the conclusion that there is no justification for the usual classifications of pemphigus. They deny the existence of a benign type, and are of the opinion that pemphigus is a clinical entity which has different phases, all of which

(1) Jour. Cutan. Dis., December, 1918.

may go over into another or coëxist. All of the various forms are invariably fatal, and in this respect the disease differs from others, the lesions of which simulate it. The imitators are dermatitis herpetiformis, erythema bullosum, urticaria bullosa, vaccinia, and their sub-varieties. None of these is fatal except the bullous dermatitis described by Engman and Mook, which follows vaccination, and which in many respects resembles pemphigus.

A tabulation of the cases shows that the bullous form commonly called pemphigus vulgaris occurs most frequently. Of thirty cases, twenty-two were of this type. The foliaceous lesions were associated with the vulgaris type in one case, and the vegetating lesions occurred in four cases of this type. Thirteen males and seventeen females were afflicted. It is a striking fact that eleven of each sex had pure pemphigus vulgaris, whereas of the rarer forms six were in women and only two in men. All the cases occurred in adults; six were in the third, three in the fourth, seven in the fifth, six in the sixth, seven in the seventh and one in the eighth decade. With the exception of one Italian, all of the patients were Hebrews from southern Europe, or whose ancestors came thence. Fourteen were born in Russia, six in Austria, four in the United States, two each in Roumania and Hungary and only one in Germany.

The fact that of the thirty cases, twenty-three first showed lesions in the regions exposed to trauma, that is, the nasopharynx, head and face, lead the authors to conclude that trauma may be a predisposing factor in the etiology. In sixteen cases the mouth was first involved, in two the mouth and throat, in one the scalp, in four the face and in seven the body. One patient acquired the disease after extraction of a tooth, and the dentist is now being sued for damages.

With the exception of three patients, one of whom committed suicide, and two who are still under observation, all died. Of the twenty-seven fatal cases, seventeen died within six months, seven more between seven and ten months, and three between the eleventh and eighteenth months. Death resulted mainly from cachexia, occasionally from pulmonary edema, but

never from any direct manifestation that might explain the disease. From these facts it would appear that pemphigus is invariably fatal, and that any disease which appears to be pemphigus and is not fatal is not pemphigus.

In two of the thirty cases, the temperature was not recorded. Of the remaining twenty-eight, there was no fever in fifteen, only a slight elevation in five, a fever ranging from 101° to 103° F. in five, and in three cases it ran from 103° to 104° F. In one case in the last group the temperature was normal until abscesses appeared in the axilla, and it returned to normal after the evacuation of the abscesses. Thus, in twenty-three of the twenty-eight cases it may be stated that there was no fever. When fever is present it is irregular, rises sometimes in the forenoon and sometimes in the afternoon, often appears when the rash is at its lowest ebb and vanishes when the bullae recur.

There was no uniformity in the blood picture. In only four cases did the leukocytosis exceed 16,000; in eleven it ranged from 11,000 to 15,000, and in six from 8,000 to 10,000. In three cases there was no leukocytosis. In only one case was there a polymorphonuclear leukocytosis about 70 per cent. and in only four was there an eosinophilia. The figures in these cases ranged from 12 to 32 per cent. The eosinophilia, therefore, appears to have no distinctive bearing on the condition.

The necropsies were prevailingly negative, particularly as regards the intestinal tract. Inasmuch as the disease frequently has its onset in the mucous membrane of the mouth it is strange that the gastro-intestinal tract does not more often show more involvement.

In the treatment, everything was attempted. Arsenic, arsphenamin, lipoids, proteose, vaccines, autoserum and quinine were all given, chiefly intravenously. Blood transfusions were also tried without avail. The disease followed its course, improving or relapsing, without any relation whatsoever to the treatment. One patient was given the adrenalin treatment as advocated by Samberger. For a short time there was marked improvement, but a few days later the patient suddenly died.

Another patient was given morphine and codeine for the purpose of suspending catabolism as much as possible. This was also attended with failure.

Concerning the etiology, the authors have very little to offer. The infectious theory, both general and focal, has its limitations. The disease is usually afebrile, but so is tuberculosis as a rule, until secondary infection takes place, and syphilis is nearly always except in the marked cases of the secondary stages. The frequency of the onset in the mouth, however, favors infection, but if it be an infection it is not an organism of the streptococcus or of the pneumococcus groups, nor is it a spirochete or protozoon because of the lack of any therapeutic results in the use of arsphenamin. It is not unreasonable to accept as a working hypothesis the theory that the disease is infectious, and inasmuch as the onset is usually in the mouth the home of the organism must be there.

Pemphigus in an Orang-Utan. An interesting eruption, closely simulating pemphigus, was observed in an orang-utan by F. D. Weidman.² The duration of the disease was about seventeen months. The animal died of advanced caseous tuberculosis of the lungs, liver, spleen and lymph glands.

Vesicles and blebs, some of which were as large as a bean, were distributed over the extensor surfaces of the arms and forearms and over the dorsa of the hands. Similar lesions were found over the corresponding parts of the legs and feet, and over the trunk and neck. The bullae were invariably tensely distended with fluid which was usually clear at first, but later became turbid or hemorrhagic. The lesions tended to occur in groups, and according to the keeper, were without subjective sensation. No involvement of the oral mucosa was observed at any time. It was estimated that probably about a dozen attacks with incomplete remissions had occurred.

Two forms of eosinophiles were found in the serum, but it is not mentioned whether they were found in the serum of the bullae or in the blood serum of the animal. No leukocyte count, or differential count is reported.

(2) Jour. Cutan. Dis., March, 1919.

Skin Lesions and the Blood System. In the opinion of Douglas Symmers,³ the association of a certain group of exfoliating dermatoses with lesions of the lymph nodes implies a broader significance than that of a toxic tuberculide, as maintained by Jadassohn. He also believes that the members of this group, together with certain other skin conditions, are but the externalization of toxemias of lymphoid, possibly, also, of medullary origin, into which tuberculosis may or may not enter, as the case may be.

For descriptive purposes, the disorders of the skin associated with diseases of the hemopoietic system may be classified, broadly, into (*a*) those in which the skin is the seat of infiltrations of identical cellular composition with the changes in the hemopoietic tissues themselves; and (*b*) those in which the skin is involved by a diversity of changes, such as simple prurigo, urticaria, pigmentations and desquamative dermatoses, all of them expressive, no doubt, of local disturbances brought about by toxic substances manufactured in the deeper tissues and offered to the skin for excretion.

Instances of generalized exfoliative erythrodermia occur sufficiently frequently in association with such diseases of the lymph nodes as Cohnheim's pseudoleukemia, lymphatic leukosarcomatosis, Hodgkin's disease, mycosis fungoides and disseminated tuberculous lymphadenitis, as to indicate a symptomatic relationship. It seems probable that, in these circumstances, toxic substances formed in the lymph nodes are offered to the skin for excretion, interfering with its nutrition in such fashion as to promote widespread desquamation of the superficial epithelium.

There are apparently excellent reasons for the belief that mycosis fungoides is primarily a disease of the hemopoietic system, more particularly the lymph nodes, in the course of which diversified skin changes arise, partly as phenomena secondary to the discharge of lymphotoxins or myelotoxins, or both, and partly as a result of infiltration of the skin by the same variety of cells as characterize the structure of the diseased lymph nodes themselves.

(3) Jour. Cutan. Dis., January, 1919.

The clinical and pathologic changes in the so-called lymphodermia perniciosa of Kaposi are essentially the same as those of Sternberg's lymphatic leukosarcoma; both belong in the category with cases of mycosis fungoides in which leukemic transformation occurs.

The greater number of all cases of so-called sarcoid growths, as grouped and classified by Darier, are almost certainly nodular cutaneous tuberculomas. The term sarcoid should be eliminated from dermatologic literature as meaningless and confusing.

Keratolysis Exfoliativa. Attention is called by G. W. Wende⁴ to a benign, non-inflammatory disturbance of the skin to which the author gives the name of keratolysis exfoliativa. It is characterized by circumscribed exfoliating patches of the superficial epidermis, usually symmetrically distributed on the palms and soles, and occasionally on the dorsal surfaces of the hands and feet, as well as on the legs and arms. The disorder is often associated with chronic eczema and eczema seborrheicum, and it is frequently mistaken for a manifestation of these diseases. Sometimes it is seen in connection with hyperidrosis and dysidrosis and other conditions involving the palms and soles. Of much interest is its occurrence in cases of eczematoid ringworm of the extremities. The desquamation begins as a minute spot and gradually extends peripherally, producing a whitened epidermis which is soon detached. There is a tendency to relapse and recurrences take place at intervals of a few months to years. Microscopic examination of the tissue from five cases showed no fungus to be present (Plate XV).

The etiology of this condition is obscure; it is often associated with inflammatory diseases which are characterized by desquamation, and irritants often produce an exfoliation which very markedly resemble it.

Cases similar to those described by Wende have been seen by J. E. Lane,⁵ who has long been familiar with the affection, and who has always classed it as *desquamation estivale en aires des mains*. This was first described in 1903 by Caragin of Dubreuilh's clinic.

(4) Jour. Cutan. Dis., March, 1919.

(5) Ibid, April, 1919.

Caragin described two forms of the affection; one very common in which the desquamation is very slight and in which cure takes place in two or three days, though often promptly followed by recurrences; the other in which the desquamation is greater and in which cure takes place only after several weeks. This form is also frequently followed by a recurrence.

During recent years, Lane has observed a considerable number of these cases. All were seen in the summer and all cleared up with the approach of cold weather. There was never an attendant hyperidrosis or dysidrosis. In several cases, seasonal recurrences had been noted and one man of 40, in good health, had had marked attacks for four successive summers. The palms are the sites most frequently involved, but the soles and the dorsi of the hands, as in Wende's cases, were sometimes seen to be affected.

The treatment of the mild cases consists in the application of simple ointments. In the severe cases application of a mild dose of Roentgen ray should prove effective in bringing about a prompt cure, as was the result in one of Wende's cases.

Psoriasis and Diet. The work of Shamberg and his co-workers showing that there is a marked retention of nitrogen in psoriatics led logically to the conclusion that a withdrawal of proteins, or nitrogenous foods, from the diet of such patients, would benefit them. This phenomenon was demonstrated, not only by the discoverer, but by many other clinicians as well.

W. A. Pusey⁶ reports a case of psoriasis observed in a young woman who had been a partial vegetarian since childhood. "For the last four years she has eaten a very small amount of meat, nothing but pork chops and beef; she eats sparingly of these and never but once a day, her reason being that she does not care for meats.

* * * She is very fond of gravies."

[In his original communication, Shamberg pointed out that merely a reduction of nitrogenous food was not sufficient to cause a disappearance of the lesions of psoriasis. He found it necessary, on the contrary, to hospitalize his patients in order that the food might be

(6) Jour. Cutan. Dis., April, 1919.

weighed and controlled and the nitrogenous foodstuffs thereby reduced to the required minimum. Very few patients have the strength of will, or the understanding of the importance of the strict adherence to instructions which are necessary to attain the desired results. A patient eating "sparingly of these and never more than once a day" is not, according to Shamberg's conception, on a protein-free diet, and that patient might as well eat as much protein as desired, because no therapeutic effect will be noted. Therefore it would appear that the case reported by Pusey is not necessarily evidence tending toward the view that the absence of protein in the diet is of no value in the treatment of psoriasis.—M.]

Bromidrosiphobia. There exist a few small groups of nervous and mental disorders which involve the skin only secondarily, and which can not logically be classified with the true neurodermatoses. Despite this fact, it is on the dermatologist that the responsibility of their clinical recognition largely rests. The more common of these affections, such as trichotillomania and trichokryptomania belong in the category of "tics," or habit spasms. Next in frequency of occurrence are some of the various fear psychoses, which are characterized by a morbid dread of parasitic contamination, and of which acarophobia and syphilophobia are typical examples. By patient and careful questioning, one can occasionally uncover the basis on which a fear of this kind rests, and if the patient is sufficiently intelligent, the possibility of infection ever having taken place can be explained away. R. L. Sutton⁷ encountered a phobia of a different type in which the fear was directed against an odor instead of an organism.

A fairly intelligent man of 63, a retired farmer eighteen months prior to the date of the first examination had developed an itchy disorder of the trunk. This affection had persisted for a fortnight or longer, but finally disappeared, leaving no trace. A few weeks later, the presence of the troublesome odor first became apparent. The trunk and axillae were primarily involved, but the area from which the "disagreeable emanation,"

(7) Jour. Amer. Med. Ass'n., May 3, 1919.

as the patient rather grandiloquently called it, arose, gradually passed downward and for the last twelve months had been confined to the feet and ankles.

He described the odor as of variable character. At the onset, it resembled that of "rotten onions," but at the time of the first consultation he thought his feet smelled as if he had not washed them for many months, although they had been bathed twice on that very day. He said that as a result of the constant and disagreeable odor, his friends had practically deserted him, and his children (he is a widower) did not care to have him come to their homes.

The skin on all parts of the body was found to be normal for that of a man of 60. The soles were pink, soft and moist, and there was no exfoliation or maceration of the epidermis in the interdigital areas. There was no evidence of hyperidrosis. The patient's shoes, which had been worn for several weeks, were no more odorous than those of an ordinary individual.

Prurigo Lymphadenique. A case resembling malignant granuloma of the Germans, or lympho-granulomatosis studied by Dubreuilh under the title "*Prurigo lymphadenique*," was seen but not very carefully studied by Hudelo and Chabanier.⁸ The patient was a woman 27 years old, without any special antecedents of interest in the case. About fifteen months before she was first seen there developed in the left cervical region tumefactions which a few weeks later invaded the axillae. These gradually increased in size until they became large masses encircling the neck and filling the axillary spaces. The mediastinal lymph glands were involved and there was a marked edema of the mammary glands. Examination of the blood showed a moderate anemia and a leukocytosis of 22,500. The skin was covered by a papular eruption which in places became vesicular. The papules averaged a millimeter in diameter and were badly excoriated and crusted. The excoriated papules had left numerous scars.

Generalized Vaccinia with Horse-Pox. A case of generalized vaccinia by auto-inoculation from horsepox

(8) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 3 and 4.

is described by Fernet and Scheikevitch.⁹ The patient was a man 75 years old who had been in charge of sick horses. For fifteen days prior to coming under observation he had had cutaneous lesions, the first one of which had appeared in the left hand. Very rapidly these lesions had become generalized. When seen the lesions were on the arms and particularly about the axillae and on the chest. There were very few upon the back and abdomen and upon the legs. The lesions were polymorphous and of different stages of evolution. Some were well-filled vesicles, whereas others were umbilicated with a red areola. Still others were frankly purulent. There were numerous crusts which represented the oldest of the lesions.

Acute Striae Atrophicae following Influenzal Pneumonia. The occurrence of striae atrophicae unconnected with stretching of the skin such as occurs in pregnancy, edema or obesity is not common. During the epidemic of influenza in 1918 and 1919, Cockayne¹ saw three cases at the Royal Naval Hospital, Haslar. In all three cases striae atrophicae were bluish-red in color and depressed below the surfaces of the neighboring skin. In no case was any pain complained of. In one case, the striae were unilateral and confined to the diseased side; in one case they were symmetrically placed on both sides, though the disease was much more severe on the right side; and in the third they were much more marked on the side on which the pneumonia had been worse.

In all three patients, physical condition was good on admission, and they were not unduly fat. None had any edema during their lives. Striae atrophicae developing during acute illnesses have been recorded by a number of authors. They are most often encountered on the legs or abdomen in enteric fever; less frequently in scarlet fever and other febrile diseases.

Shepherd gives an excellent figure of striae atrophicae round the knees in a boy who had had enteric fever and Dyce Duckworth describes a similar case in a boy, aged

(9) Bull. Soc. franc. de dermat et de syph., 1919, Nos. 3 and 4.

(1) Brit. Jour. Dermat. and Syph., April-June, 1919.

PLATE XV.



Keratolysis exfoliativa. Peeling began in the hands and then extended to the interdigital surfaces of the fingers.—Wende, page 92.

PLATE XVI.



Transverse hyperpigmented lines in a negro infant.—Weidman, page 102.

15 years, who developed them on the outer side of the left thigh and near the malleoli.

Parkes Weber has written an interesting note on striae patellares in appendicitis, and acute osteomyelitis, in which he points out that the stretching of the integument of the knees in the flexed position assumed in the former illness is a most important factor in their production. He also lays stress on the fact that most of the cases occur about the age of puberty, and the rapid growth, which often takes place during early convalescence, causes a strain on the weakened skin. As examples of other diseases in which they appear, one may quote Graham Little's case, in which they followed mumps complicated by orchitis in a boy, aged 16 years, and Plagge's, in which they appeared on the abdomen of a case of typhus fever.

Troisier and Menetrier proved microscopically that in their case there was an actual rupture of the elastic fibers of the skin. There can be no doubt that the mechanical factor invoked by Parkes Weber plays an important part in their production by causing rupture of elastic tissue weakened by the toxins set free in various fevers. There is probably still another factor concerned in the etiology of this condition, and that is a weakness in the elastic fibers themselves which is present prior to the illness, and which makes them more susceptible to the action of a toxin. This is supported by the fact that a few cases have been recorded in which striae made their appearance in healthy individuals after a period of very rapid growth. The diseases which cause the condition are so varied and so common that it would be met with much more frequently were this not the case.

The toxin which in these cases weakened the fibers must have been due to the influenza, or much more probably to the secondary streptococcus infection. With regard to the mechanical factor, it is interesting that the patient with most of the striae on the chest was nursed in the prone position, and the two in whom the striae were low down were nursed for the most part propped up in bed.

Poikiloderma. A case presenting a very unusual

skin eruption for which the term "*poikiloderma atrophicans reticularis*" was proposed by Jacobi, was studied by Civatte and Eliascheff.² The patient was a woman 41 years old who had had a dermatosis for five years. It began on the nucha and had been preceded by mild subjective sensations for some time. It later spread to the face and to the arms, and became associated with a moderate degree of pruritus. When seen by the authors, the dermatosis occupied the nucha and the sides of the neck, rising up and involving the ears and the mastoid regions, also the cheeks and the temples. The midline of the face and neck was spared. The eruption stopped at the hair line of the scalp and at the base of the neck below. It extended, however, to the pectoral regions and the shoulders.

On the neck the eruption consisted of small macules averaging about the size of the head of a pin. Interspersed among the papules were areas of normal skin of approximately the same dimension. The macules were of a brownish to bluish color and in places were dotted with bright red telangiectatic points. Under pressure the color disappeared, leaving a pigmentation which suggested ephelid or lentigo. In the mastoid region there were large plaques in which there were few areas of normal skin. These pigmented erythematous plaques were covered with a multitude of small, slightly elevated points which represented the sebaceous glands. On the temples and in the region of the scalp the erythematous element was lacking. Here there were brownish areas in which there were ivory-white regions of atrophy. The atrophy, however, was very superficial and the follicular orifices remained intact. Neither was there any loss of suppleness of the skin. On the shoulders, arms and forearms the superimposed livedo was so marked that it was necessary to efface it with pressure in order to distinguish the veritable eruption. In these regions this consisted of very small and shining macules, slightly depressed, without varicosities, and without any apparent connection with the passive congestion.

The authors find it difficult to place the eruption in

(2) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

any other category than the one named. They were able to eliminate an arsenical dyschromia and radiodermatitis inasmuch as there had been no arsenical medication and no radiotherapy. Morphea, lupus erythematosus, lichen planus, and all the cicatricial dyschromias are too limited in their extent to be confused with this diffuse dermatosis. Moreover, the atrophy had not been preceded by any other affection.

The first case of this kind was described by Petges and Clejat in the *Annales de dermatologie et de syphiligraphie*, in 1906. A dozen such cases have been described since that time in Germany.

Poikiloderma may be summarized as an eruption primarily of the face and neck; the trunk and arms are attacked less frequently. Only one observation has been made of a lesion on the thigh. The eruption is seen ordinarily on the face in the form of plaques and on the neck in the form of a reticulation. This reticulation is pigmented, covered with varicosities and slightly atrophic. The eruption is pruritic and is years in developing. Concerning the etiology nothing is known at the present time and it must be grouped with the idiopathic atrophies and sclerodermas.

Histologically, the sections showed a superficial atrophy. In places this was complete and in others in a state of evolution. In the former the papillary body was flattened and in the latter there are seen considerable islands of incompletely atrophied skin.

In the opinion of Darier the dermatosis was probably a pigmented syphilide.

Sclerema of an Adult. A generalized scleroderma involving practically the entire skin of a patient is reported by Darier, Ferrand and Mircouche.³ The authors use the term "*sclérémie*" to designate the generalized scleroderma or edematous scleroderma of Hardy which involves the trunk and face and the limbs but not the fingers and toes. The skin was so hard that neither could superficial papillary folds nor deep folds involving the entire derma be produced. There were two stages of evolution of the scleroderma: namely, the hard,

(3) Bull. Soc. franc. de dermat. et de syph.. 1919, Nos. 5 and 6.

edematous infiltration and the subsequent atrophy. Along the left arm was a scarcely visible but definite and typically waxy line representing the scleroderma of the band-like type. There was no cutaneous pigmentation. The sclero-edematous areas had the usual violaceous color and the sclero-atrophic areas the typical appearance of old wax. There were verrucous points and hyperkeratotic points about the folds of the elbows and axillae. Histologically, there was a condensation and sclerosis in the papillary body accompanied by a perivascular edema in the corion. There was indication of an extensive connective tissue proliferation and an absence of any indication of connective tissue inflammation or degeneration which has been observed in the plaques of morphea.

An Unusual Case of Psorospermiosis (Darier's Disease). A case of psorospermiosis in a man 62 years old which began with a vesicular eruption closely resembling weeping eczema is reported by Fernet and Scheikevitch.⁴ After the vesicular lesions had been present for some time brownish, adherent crusts characteristic of the disease appeared. The development of Darier's disease in a vesicular eczema associated with weeping and pruritus is quite unusual. As a rule, the disease comes on between the eighth and sixteenth years, but in this case it appeared at the age of 60 years. On the hands of the patient were congenital verrucous lesions which were probably verrucous nevi.

Examination of the sections by Darier confirmed the clinical diagnosis.

Pustular Dermatitis Herpetiformis. Brocq states in the "*Traité élémentaire de dermatologie*," that he has never seen pustular dermatitis herpetiformis, despite the fact that Duhring maintained that such cases had been seen by him. Milian⁵ studied the case of a soldier 32 years old who came to the dermatologic center with the diagnosis of eczema. On the trunk were miliary pustules, crusts and macules, which were grouped in such a way that a syphilide was immediately thought

(4) Bull. soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(5) Ann. de dermat. et de syph., July, 1919.

of. A Bordet-Wassermann test having been found to be positive, without further study the patient was given a series of intravenous injections of arsphenamin. In spite of four injections, however, there was no change in the eruption. After the failure of the therapeutic test the patient was carefully studied and it was found that the lesions had been coming in a series of crops. The attack which the patient was then in had been present for two months, and he had had several attacks in the preceding three years. The elementary lesion was a pustule from the beginning. The author was able to watch these develop on the surface of the purpuric skin, which was the site of former crops. At no time was there a vesicle or bulla present. The lesions came on in crops of from ten to twenty on the trunk and on the arms without any marked subjective sensation. They were associated, however, with slight elevation of the temperature during the onset. The pustules were about the size of the head of a pin and were never umbilicated. They never developed upon normal skin, but always upon purpuric spots. Interspersed with these bullous lesions were psoriasiform lesions, somewhat copper-colored, which represented the terminal stage of the pustular groups. The contents of the pustules showed many polynuclear leukocytes, a few mononuclear leukocytes and epidermal cells. There were no eosinophiles present; there was, however, an eosinophilia of 4 per cent. in the blood.

The author bases his diagnosis of dermatitis herpetiformis upon the following facts: The pustules appeared in successive crops; the evolution of the lesions showed the same progressive dessication, with the same purpuric relics; the distribution was similar to that of dermatitis herpetiformis, being localized in the folds of the skin and recurring in the same areas; there was an eosinophilia of 4 per cent., and there was an infiltration of eosinophiles in the sections studied. The pustule was found to be situated between the corneous layer and the mucous layer of the epidermis, as it is in dermatitis herpetiformis.

An Unusual Case of Granuloma Annulare. A case of granuloma annulare lacking the usual ringed arrangement of lesions, with the lesions on the elbows instead

of on the hands, and occurring in a patient who had a positive Bordet-Wassermann reaction is reported by Stillians.⁶

The patient was a robust woman 28 years of age. Over each elbow was a round pad, 0.5 to 1 cm. thick and about 3 cm. in diameter, of a doughy consistence, containing three or four flat, hard plaques, roughly oval, from 0.5 to 1.5 cm. in length. On these pads were groups of round papules, 0.2 to 0.5 cm. in diameter, hard and only slightly elevated, so that it was only by stretching the skin that some of them appeared distinctly papular.

Some of them were of normal skin color, but most of them were of a faded, old rose color, many with yellow centers. Several larger oval papules up to 1 cm. in length had been formed by coalescence of two or more of the round papules. There were eighteen papules on the right elbow and about ten on the left. There were other deep flat nodes similar to those in the elbow pads, movable with the apparently normal skin covering them, one over each tendo Achilles, one just below the right knee, one on the left shin, one just below the left and another above the right elbow. Below the right elbow were two in a line extending from the olecranon to the wrist, making a total of forty-three. All were hard, most of them giving a sensation of cartilage, but some of the papules felt like shot. The grouping and yellow color led to a provisional diagnosis of xanthoma tuberosum.

[We have had a typical case under observation for the past two years. There is one large ring on the dorsum of the right hand and numerous solitary lesions scattered about the hands and arms. A lesion excised for biopsy never recurred. Excellent results have been attained with carbon dioxide snow. The patient, however, lives in another state and allows many months to elapse between visits, thereby giving new lesions plenty of time to develop into large lesions before treatment.

The section showed the typical necrotic mass with radiating cells.—M.]

Hyperpigmented Lines on the Trunk of a Negro Infant. A moribund negro infant entered the University Hospital in Philadelphia and died before a history was

obtained. At autopsy, F. D. Weidman⁷ discovered transverse, hyperpigmented lines across the thorax and abdomen.

The lines were at first regarded as due to dirt which had collected in skin creases along lines of body flexure, but it was quickly noted that there was in addition a very distinct linea nigra from the umbilicus to the pubis, and that the lines extended to a level well upward over the ribs (a rather rigid foundation over which flexion is not to be expected); and, finally, vigorous rubbing did not efface them. For these reasons it was concluded that they were really in the skin and deserved special study.

As shown in the illustration (Plate XVI), the lines begin 18 mm. below the level of the nipples, are spaced at regular intervals of from 8 to 10 mm.; are ten in number and cease about 2 cm. above the pubis. Laterally, they reach fully to the midaxillary line.

Microscopic sections were made first to determine the nature of the pigmentation, and secondly with the thought in mind that the lines might represent the cutaneous junction of embryonal segments and that under them nevoid cells might appear in a form which would throw some light on the debated genesis of pigmented nevi.

The histologic examination showed that the lines are referable to an excess of the ordinary melanin pigment in the rete with no changes in the corium.

A detailed examination of the rete showed that the grade of pigmentation was irregular along different stretches lateral to the crease, and that some groups of cells here contained as much pigment and were pigmented in just as great numbers as those in the crease. This means that the crease was darker grossly, not because its cells contained more pigment granules than those elsewhere, but because here there was no microscopic alternation of highly and lightly pigmented stretches such as were seen on either side. Or, put in another way, the deep color in the crease was not diluted by the interposition of occasional lighter stretches.

Out of the histologic studies has come a practical

point. Weichman and his associates were very much surprised when the first set of histologic sections came through by the paraffin embedding method, to find that there appeared to be no excess of pigment in any part of the skin and they set about to determine why there should be this grossly but not microscopically recognizable pigmentation.

It was found that some, but not by any means all of the pigment is dissolved out or altered in the paraffin technique, and that it is better to use the frozen section method when studying finer matters of pigmentation. It might be mentioned in passing that Stevenson has found an allied melanin soluble, reporting that acid-alcohol dissolves malarial pigment in from 5 to 8 micron sections, and that this fact is useful where it is so abundant as to obscure tissue details which are proposed to be studied. But it certainly does not dissolve skin melanin as fully as Stevenson indicates for malarial pigment.

Elephantiasis in a Female. A patient 40 years of age, with a tremendous elephantiasic edema of the pudenda was observed by Lt.-Col. Bryson.⁸ She had menstruated fairly regularly and had borne three children, the youngest of whom was four years of age. The duration of the growth was ten years. The clitoris and the urethra could be palpated without difficulty.

Elephantiasis Vulvae. A case of elephantiasis of the external genitalia is described by Ravogli.⁹

Elephantiasis of the typical form is endemic in certain tropical and subtropical countries where it has been found to be the result of the entrance into the system of a parasite, *Filaria sanguinis hominis* (Lewis).

In this country we encounter the false or non-parasitic elephantiasis. The parts are enlarged because of the enormous increase of the connective tissues forming the derma, and the subcutaneous tissue elements. It is due to the stasis of the lymph in the lymph spaces from an obstruction of the lymphatic vessels.

This condition is occasionally observed following syphilitic gummas and long-standing ulcerations of syphilitic and tuberculous nature, causing stasis of the

(8) Indian Med. Gaz., June, 1919.

(9) Jour. Cutan. Dis., January, 1919.

PLATE XVII.



Elephantiasic enlargement of the vulva following syphilitic infection in a patient with chronic gonorrhea.—Ravogl, page 104.

PLATE XVIII.



Same patient after operation.—Ravogl, page 104.

lymph spaces and, consequently, a hard, permanent edema. One sees cases of elephantiasis of the genitals in the male, but more frequently in the female, especially in old prostitutes suffering with a chronic ulcerative syphilide. The disease occasionally occurs in white females, but more often in colored women.

Ravogli's patient was a colored woman 28 years of age, who had had syphilis for three years. The urine was negative and the Wassermann test was positive. No gonococci were found in the vaginal secretion. The labia majora resembled two round, hard spheres of the size of a small orange. The left was somewhat larger, oval in shape, the surface uneven, with hard papillomatous granulations emerging from the principal mass. Between the granulations were grooves which were moist, exuding serum. The clitoris was enlarged and elongated in the form of a triangular tumor, formed by a mass of granulations of the size of small cherries. The clitoris was compressed between the enlarged labia. At the posterior commissure, a round tumor protruded between the labia; this was hard, well limited, and similar to the other tumors (Plate XVII).

The clitoris was removed just at the point where the prepuce is in contact with it. Then the labia were removed by means of two incisions, one at the external and one at the internal side. The incisions were made from below upward so that when the tumors were ablated the remaining skin formed an angle. Finally the tumor at the posterior commissure was removed. The blood-vessels were tied, and the surfaces of the wound were sewn together with catgut (Plate XVIII).

[Despite the presence of syphilis as shown by the history and the positive Bordet-Wassermann reaction, no intravenous injection of arsphenamin was given.—M.]

Sparganum (Larval Cestode) in the Subcutaneous Tissues. The occurrence of *Sparganum*, the larval form of members of the *Bothriocephalidæ* family of tapeworms, is rare in man. In Manson's work on "Tropical Diseases." *Sparganum* (*Bothriocephalus*) *mansoni* (synonym *Bothriocephalus liguloides*) is mentioned. This worm, which was first discovered by Manson himself, lying under the peritoneum in the neigh-

borhood of the kidneys and iliac fossae in considerable numbers, measures in the original specimens about 30 to 35 cm. in length by about 2.5 mm. in breadth. Manson (1903 edition) also refers to one of the Australian records of the presence of *Sparganum* in man. As a matter of fact there are already two records of finding *Sparganum* in human beings in Australia, while the one now recorded by J. B. Cleland¹ makes the third definite case. In all Australian instances, the parasite has been much smaller than that found by Manson, measuring from about 3.5 cm. to about 10 cm.

About a year before the specimen was found, the patient who was a business man in Sydney, had noticed a small hard swelling on the front of the leg, which remained about the size of a small Barcelona nut for a considerable time. It then became inflamed and tender and discharged a little pus, but the inflammation finally subsided. When the scab over this area was removed the specimen came away. The patient had not lived in any country districts, but he had spent every week-end for years at a camp in Middle Harbor, Sydney.

The specimen as submitted was white, flattened, and almost like a piece of tape, and about 5 cm. long and nearly 1 mm. broad at its broadest point. With a hand lens, one end was seen to be frayed, having evidently been broken off, while the other end, which seemed injured, was bluntly truncated. With a low power of the microscope the body was found to be indistinctly striated longitudinally; no segmentation could be detected, and at the complete, though injured end, no grooves could be seen. Scattered throughout the body were oval, concentrically marked bodies. Microscopically, the section of the parasite showed a rather thin cuticle, which was succeeded by a layer of nuclei, lying at right angles to it. The parenchyma showed occasional delicate fibers with widely scattered small nuclei, and moderate numbers of concentrically marked calcareous corpuscles. These were about 8 or 9 inches in length and showed a central nucleus. The various body layers were not nearly so distinct as in the *Sparganum* from *Varanus*, received from Dr. Nicoll.

(1) Med. Jour. Australia, Sept. 21, 1918.

The occurrence of these larval bothriocephalids in man in Australia is undoubtedly an accident in the life history of the parasite, whose normal intermediate host must be looked for in some other animal. It would seem from the description of the three Australian cases that they probably all belong to the same species and that, as might be expected, this is probably different from Manson's Asiatic one. It seems not improbable that some reptile—possibly a snake or monitor—may be the ordinary intermediate host, and this is rendered more likely, inasmuch as the Australian mammals have been fairly well searched for parasites and, no species of *Sparganum* has been detected in them. If these three cases have, more or less by accident, been recognized, it is quite possible that a number of other cases have been met with but for various reasons it has not been possible for their true nature to be discovered. The possibility of unusual inflammatory swellings in the abdomen or in the subcutaneous tissues, being due to such helminthic parasites, should be borne in mind, and possible in this way further cases may be discovered.

An Acid-Fast Bacillus obtained from a Pustular Eruption. A bacillus was cultivated by Louis Cobbett,³ of Cambridge, from chronic intractable pustules covering the back, buttocks and thighs of a soldier returned from France. No microörganism was seen in the pus, and none could, at first, be cultivated from it. But subsequently there was grown, on more than one occasion the acid-fast bacillus which is the subject of this report.

The patient, aged 24, was wounded in the foot; he returned home on a boat which was torpedoed and sunk in the early part of 1917. After being in the sea nearly an hour he was picked up and brought to England. The wound in the foot at first healed, but subsequently broke down again, and two operations had to be performed. For a fortnight he was treated in the First Eastern Hospital, Cambridge, by continuous immersion in the bath. It was about a month after this that the eruption was first noticed. The back and buttocks were covered with swellings of various sizes and

(3) Brit. Med. Jour., Aug. 17, 1918.

different stages of development; some were simply old red scars, others were just pointing and were much raised and indurated measuring perhaps as much as an inch at their bases. From one of these was obtained a stringy pus in quantity larger than one would have expected. What was particularly noticeable was the exceedingly chronic character of the inflammation and the deep-seated position of some of the lesions; for the most active pustules, though somewhat painful and tender to the touch, caused far less trouble than an ordinary boil, and spots which were watched from time to time seemed to make little appreciable progress. Moreover, there were a few swellings, distinctly fluctuating, which were completely subcutaneous, and over which the skin could be freely picked up.

The pus was examined on several occasions and various methods of staining were used, but no bacteria were ever seen in it, even when the stain was that used for acid-fast bacilli. The pus differed entirely from tuberculous pus inasmuch as the cells were well formed and showed little sign of degeneration and also were clearly defined, but contained more nuclear fragments than usual.

Cultures were attempted on various media. No visible growth appeared on egg or blood agar, or on ordinary agar cultivated anaërobically; but on agar in the presence of air five rather large cream-colonies appeared, and these were found to consist of long slender bacilli. Subsequently the same bacillus was obtained in impure culture from an aërobic egg tube.

The bacilli stained well by Gram's method. When so colored they were further treated with 5 per cent. acetic acid to see whether they possessed polar bodies. The only effect of this treatment was to bring out an irregular segmentation of stainable material like that seen in bacilli of the diphtheroid group. Polar bodies were probably present, but they were not definitely revealed. When stained with carbol-fuchsin, after the manner used for phthisical sputum, they were found to resist decolorization just like tubercle bacilli.

Grown side by side with the fish-tubercle bacillus certain differences became apparent. For while both

organisms grew well at 220° F. the new bacillus grew even better at 37° C., at which temperature the fish-tubercle bacillus refused to grow at all; and at the temperature of the cupboard—from 12° to 16° C.—the fish-tubercle bacillus grew well, but the new bacillus scarcely at all.

Vincent's Angina Simulating a Chancre of the Tonsil.

Vincent's angina is not infrequently mistaken for mucous patches of syphilis, but its appearance is rarely such as to lead to mistaking this disorder for a chancre. Clement⁴ saw a soldier who had been given a diagnosis of chancre of the tonsil, and who was about to be transferred to a venereal center. Examination disclosed the right tonsil markedly enlarged and ulcerated. The ulcer was covered with a grayish pseudo-membrane. Induration of the tonsil was pronounced, as was also the regional adenopathy of that side. The inflammatory process was limited strictly to the right side. There was no fever and no systemic disturbance. A smear of the throat showed the presence of the fusiform spirillum of Vincent. After local treatment had been continued for some time without effect, two intravenous injections of novarsenobenzol were given with immediate healing.

[In the base hospital at Fort Riley, the routine treatment of Vincent's angina consisted of gargling the throat with a solution of 0.1 gm. arsenobenzol in 100 c.c. of water. This solution was made up in the syphilis clinic fresh each day as needed. This local application of the drug was found to be much more efficacious than the intravenous administration and much less trouble.—M.]

PHAGADENIC ULCERS.

Phagadenic Genital Ulceration of Fuso-Spirillum Origin. A soldier, 40 years of age, a native of Corsica, with chronic malaria, was seen by Meurisse.⁵ While on a furlough he ran a splinter of wood into the left side of the glans penis. There was a marked hemorrhage

(4) *Ann. de dermat. et de syph.*, December, 1918.

(5) *Ann. des mal. vén.*, July, 1919.

and in spite of various local applications healing failed to take place. When seen by the author two months later there was an irregular ulceration with undermined borders on the left of the glans. The ulcer was very painful and was bathed in pus. There was also painful bilateral inguinal adenopathy. Microscopic examination disclosed the presence of the fuso-spirillum infection of Vincent. The Bordet-Wassermann reaction was negative, but in spite of this the patient was placed upon intravenous injections of cyanide of mercury, with local applications of iodoform. After about a week of the injections the patient developed such an edema of the penis that the injections were stopped. There was no improvement in the appearance of the lesion. After various methods of treatment the patient was put upon potassium iodide and after some time the lesion healed, but the edema did not entirely disappear.

It is an interesting fact that although the patient was given a number of intravenous injections of arsphenamin without improvement, the lesion seemed to heal under potassium iodide. No attempt, however, was made to treat the ulcer with local applications for arsphenamin.

Phagedenic Ulcer of Warm Climate. Malignant ulcers of the skin occur in many tropical and subtropical countries. They have been named after the country in which they occurred. The disease was first described by Vincent in 1857, under the name of *l'ulcere de Mozambique*, occurring principally among the kaffirs. Five years afterward, Capius observed the same disease in Guiana. Since then numerous writers have described it by other synonyms, *viz.*, Gabon ulcer, Aden ulcer, ulcer of Yemen, seen especially among the negroes of Sennaar, Kordofan, and Darfour, among the Arabs of Zanzibar and Massouah, ulcer of Annamite, seen in Annam and Tonkin, ulcer of Cochin-China, Congo ulcer, ulcer of Madagascar, ulcer of Guadeloupe, and ulcer of New Caledonia.

After studying descriptions of these different ulcers and comparing their characteristics, most authorities have arrived at the conclusion that they are all the same disease, called and described under the name of phagedenic ulcer of warm climates, or tropical ulcer.

The disease is essentially one of the tropics. Few, if any, genuine cases have been reported in temperate zones. The disease appears to be endemic and sporadic in the Taree district and the country drained by the Wal-lamba River, in the north coast of New South Wales, 144 miles from Sydney.

W. McMurray and F. O. Stokes⁶ collected nine cases, all of which they have seen personally. These cases are classified as follows:

Females.	Age	Affected Part.	Males.	Age	Affected Part.
M.M.	17	Right upper arm	E.G.	10	Left fore arm
F.G.	10	Right leg	G.S.	10	Left fore arm
E.T.	8	Right leg	J.N.	10	Left wrist
A.F.	Adult	Right leg	B.B.	2	Right fore arm
M.H.	6½	Left fore arm			

Eight of the patients came under observation during the past six years. The first was seen seventeen years ago but the exact nature of the disease was not then recognized. In six, the upper and in three, the lower extremities were affected—seven children and two adults were the victims. One case ended fatally. The treatment given is not mentioned by the authors in most of the cases. Arsenobenzol was tried in one of the severe cases without much benefit; later antimony tartrate intravenously was begun. This apparently was giving good results at time of writing.

The various bacterial agents to which *ulcus tropicum* was formerly attributed by different observers have now been displaced by *Spirochaeta schaudinni*, described by Prowazek and confirmed by later writers. In specimens from two of these cases spirochetes were observed under dark-ground illumination. They showed few and rather elongated coils and an active, lashing movement. Although the authors made a number of preparations they did not succeed in obtaining stained examples. The examinations revealed only pus cocci which were regarded as due to secondary infection. They did not find any bacterial microbes (*e. g.*, acid-fast bacilli) which could be looked on as having any casual relationship to the disease, nor did they find fusiform bacilli, such as

(6) Med. Jour. Australia, Feb. 1, 1919.

some authorities regard as the associates or growth forms of the spirochetes. In ascribing the disease to *S. schaudinni*, the authors are aware that spirochetes of various kinds are likely to be found as secondary invaders of open sores.

Ulcers of the Legs. Ulcers of the legs, commonly known as varicose ulcers, are, in the opinion of R. Prosser White,⁷ not due to varicose veins as a rule but to phlegmasia alba dolens. The paper is based upon a clinical review of a large group of cases of leg ulcers which were studied clinically but very little was done with laboratory tests. He finds that the ulcers are very frequently the result of post-parturition infection, and that as a rule only one leg is affected. If both legs have been the site of a white swelling the ulcers will be bilateral; and when only one, that leg will develop an ulcer. He finds that phlegmasia is twice as frequent in the right, as in the left leg, whereas eczematous ulceration may occur either in both legs or in the left only.

In the cases of ulceration following varicose veins, however, both legs suffer in equal proportions. The left leg seems to be somewhat more liable to injury and so probably develops a larger number of traumatic ulcers. The Wassermann test was not carried out in the study of these cases.

ACANTHOSIS NIGRICANS.

Acanthosis Nigricans and Cancerosis. Two types of acanthosis nigricans are now recognized. One type is known as the juvenile in which the disorder develops in early childhood, reaches a maximum and remains stationary or tends to undergo involution. The patient's health is unimpaired and there is no associated malignant neoplasm. The adult type is always associated with visceral malignant neoplasm, frequently of the stomach, and progresses to the death of the patient.

Dubreuilh⁸ saw an interesting case of the adult type

(7) Brit. Jour. Dermat., July-September, 1919.

(8) Ann. de dermat. et de syph., December, 1919.

PLATE XIX.



Acanthosis Nigricans Papillomatosi of the 3d degree.—Dub-reuilh, page 112.

Microscopically the interesting feature of the case was the cancerous invasion of the lymphatics without inflammatory reaction.

Acanthosis Nigricans. The interesting case of acanthosis nigricans reported by Dubreuilh mentioned above, in which was found histologically cancerous infiltration of the deep lymphatics of the skin without inflammatory reaction of the neighboring tissues, led Perin⁹ to make a careful study of a case which came under his observation in the hope that he might find a similar histologic picture. The patient was a woman, 46 years old, who complained of intense itching, loss of hair and malaise. She noticed in the region of the axillae and thighs pigmented areas in which there were small tumors, and stated that she had lost a considerable amount of weight during the past six months. The pruritus of which she complained had come on in the genito-crural region. The itching was almost insupportable and was most marked at night. It gradually extended until it involved the trunk and the axillae and in the past six months had reached the neck. The cutaneous changes were localized in the genito-crural region, the axillae, the neck, face and hands, gradually diminishing and ending in normal skin.

There were three types of lesions: One was a deep brown pigmentation diffuse and symmetrically placed on the body, most marked in the anterior border of the axillae. The second type consisted of papillary lesions which appeared more pronounced to the eye than to the touch. There was no loss of suppleness of the skin, but on the contrary this was rather more marked than in the normal skin. The third type consisted of small papillomatous tumors the size of a grain of wheat, sessile, smooth, without hyperkeratosis, deeply pigmented and scattered through the pigmented areas, but occasionally encountered outside of the areas of pigmentation.

In addition to the cutaneous changes the mucous membranes were also involved. The tongue was villous, with deep folds over the entire dorsal surface and a few which extended to the inferior surface. The lips were

(9) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

of a villous aspect on the free borders and the lower lip was much thickened. On the palatine arch was a horse-shoe-shaped patch of papillomatous, protruding varicosities of 2 or 3 mm. in height, which gave the mucous membrane a spongy aspect. On the mucous membrane of the cheeks, and along the gingival border the membrane was covered with papillary vegetations which suggested the tongue of a cat. The alopecia was complete.

General examination was practically negative. The patient complained of disturbed digestion and of vomiting. There was no occult blood in the stool and the urine was normal, although the kidneys were slightly palpable. The mammary glands were normal. A digital examination of the vagina disclosed nothing suggesting a neoplasm. There was nothing about the circulatory system which suggested suprarenal insufficiency. In short, there were no clinical or laboratory findings which suggested the presence of a visceral carcinosis as the origin of the cutaneous disorder. The slow onset, which had been gradual during five years, was against this supposition. However, the gastric distress and the loss of weight made it necessary to continue the investigations because of the possibility of the presence of carcinoma. Histologic examination showed no trace of cancer cells in the deep lymphatics as found by Dubreuilh.

NEVI.

Nevus Anemicus. Since the work of Vorner a number of cases of nevus anemicus have been reported. Chatellier¹ reports the observation of two cases, one of which was unusual in that the surface of the skin in the nevus area was somewhat depressed. Histologic examination showed congenital absence of blood-vessels, which confirmed the findings of other observers.

Hyperkeratotic Linear Nevus. An extensive and symmetrical linear nevus with marked hyperkeratosis is reported by Semon.² Owing to the resemblance of the

(1) *Ann. de dermat. et de syph.*, September, 1919.

(2) *Brit. Jour. Dermat. and Syph.*, October-December, 1918.

lesions to Darier's disease, Darier was asked to make a study of the section.

The most remarkable feature of the eruption, which led the writer to suspect the possibility of a totally different morbid entity, was noted on the back of the neck and slightly to the left of the middle line, in the shape of a longitudinal, almost vertical narrow band, made up of some fifty or more loosely aggregated elements.

Each of these lesions was a raised follicular papule of a dirty brown or black color. The contents were easily expressed or removed with forceps, and were of a sticky, sebaceous character, suggesting sebum and epithelial horny débris. After removal of this plug, a cup-shaped elevation remained, agreeing in the main with those described for the condition now called "*dyskeratosis follicularis vegetans*" by Darier in his "*Précis de Dermatologie*," 1918, pp. 244-5.

After a study of the sections, Darier said he thought the case to be of congenital origin, and that it resembled a case portrayed on p. 218 of the "*Précis*." He thought it probably was an example of cutaneous malformation of the order hyperkeratosis ichthyosiforme (which Brocq calls *Erythrodermie congénitale ichthyosiforme avec hyperépidermatrophie*). It is peculiar and remarkable in view of two characteristics:

Instead of being generalized, as is usually the case, the malformation shows a tendency in certain areas to assume the distribution of linear nevus, or ichthyosis follicularis, briefly described on p. 448 of the "*Précis*."

The presence of acantholysis is exceptional, though Darier has seen it in an unpublished generalized case of his own.

He suggested the following nomenclature:

"*Hyperkératose ichthyosiforme partielle à distribution de nevilineaires, et à structure acantholytique.*"

NEOPLASMS.

Subcutaneous Tumors Simulating Sarcoid due to Camphorated Oil. Sarcoid-like tumors of the subcutaneous tissue of the thigh following the injection of cam-

phorated oil are described by Brocq, Belot and Stan-kewitch.⁴ The patient was a young woman 29 years old who, in 1913, underwent an appendectomy. At this time she was given a series of injections of camphorated oil. In 1917, she first noticed in the region where the injections had been given the formation of small tumors which had become painful. These grew rather rapidly and in the course of the following year became large masses. When the patient was seen by Brocq, she was advised to have electrolysis. This method of treatment, using the negative pole, was instituted with excellent results. The needle was passed into the tumor and the decoloration about the needle was used to indicate the amount of treatment necessary.

In the discussion which followed the presentation of these cases, Darier stated that the use of vegetable oil as the vehicle for the camphor would produce these tumors as readily as the use of liquid petrolatum.

[At the joint meeting of the St. Louis Dermatological and Chicago Dermatological Societies, October, 1919, a series of cases of tumor masses following the injection of camphorated oil in pneumonia was presented by Dr. Mook. An analysis of the camphorated oil given to these patients showed that the base was liquid petrolatum. The oil had been supplied to the hospital by one of the well-known pharmaceutical houses. The masses were large, very firm, sharply demarcated and had all the appearance of paraffinomas.

The use of liquid petrolatum as a vehicle for mercury salicylate is quite common. We frequently see tumor masses which persist for some months after the injection of the mercury salicylate into the deep muscles of the buttock, but as yet we have seen no paraffinomas resulting from these injections. It may be that the intramuscular injection of paraffin oil is not conducive to the formation of the paraffinoma as it is when given subcutaneously.—M.]

Camphorated Oil Tumors. Ever since paraffin has been injected subcutaneously to remedy various defects we have been well acquainted with the possible subse-

(4) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

quent tumor development and activity. The production of similar tumor masses as the result of the injection of camphorated oil, however, is a recent observation. Mook and Wander⁵ have observed a series of tumor masses, closely simulating sarcoids of the Darier and Roussy type, which resulted from injection of camphor in liquid petrolatum as a stimulant in influenza. The first case was seen in 1914 and was studied histologically. The histologic picture was that of the paraffinoma described and studied by Hyde and others. The camphorated oil was supplied by a pharmaceutical house and has apparently been used in a great many cases. It is well known, however, that only in a small percentage of cases in which paraffin has been injected do the paraffinomas develop. The oil enclosed in the connective tissue neoplasm was found, by staining methods, to be a mineral and not a vegetable oil.

[The nodules produced by the subcutaneous injection of camphorated oil are perhaps more commonly observed in Paris than in this country, inasmuch as Darier in his "*Précis*," second edition, p. 292, compares the appearance of the Darier-Roussy, or the hypodermic sarcoid, to that of the nodules produced by such injections. As was brought out in the discussion following the reading of the paper of Brocq (pages 116-117), injection of camphor in a vegetable oil will cause the tumors quite as readily as when it is dissolved in a mineral oil.—M.]

Multiple Benign Basal-Cell Epithelioma and Sarcoma of the Scalp. Numerous examples of tumors of the scalp are recorded in medical literature. Crocker grouped most of these cases under the heading of "sarcoma capitis or endothelioma capitis (turban tumors)." A further examination of these cases indicates that they probably belong to only two classes: those which arise from the epidermis, and are basal-cell epitheliomas, and those which originate from the subcutaneous tissue, and are sarcomatous. It is probable that no case of genuine endothelioma capitis has yet been published.

H. G. Adamson⁶ reports an interesting example of each of these types of tumors. The case representing

(5) Jour. Amer. Med. Ass'n., Nov. 1, 1919.

(6) Brit. Jour. Dermat. and Syph., July-September, 1918.

the first class of tumors occurred in a patient 61 years of age. There were about fifty tumors on the scalp which varied in size from that of hemp seed to that of a chestnut. They were firm, with a smooth surface the color of the surrounding skin, devoid of hair, and movable on the skull. The lesions had been present on the scalp for twelve years but similar lumps had been noticed on the back for thirty years.

Histologically, the tumors were found to consist of sharply circumscribed alveoli, rounded, oval or irregular in shape, and surrounded by a clear hyalin stratum. The cells which made up these masses were rounded or oval, with large deeply staining nuclei. The appearance was that of a benign, basal-cell epithelioma, and was identical with that of Brooke's "*Epithelioma adenoides cysticum*."

Dubreuilh and Auché have clearly demonstrated that the cases of multiple tumors of the scalp which had hitherto been known as "endothelioma capitis" were really of the nature of basal-cell epitheliomata, and a study of the published examples of endotheliomas of the scalp, and those of Brooke's epithelioma adenoides cysticum shows that they belong to the same group. The histories of the published cases of the supposed endotheliomas show that in many instances several members of the family were affected.

The sarcomatous tumor of the scalp is apparently very rare as only two published cases can be identified as "sarcoma capitis." Adamson's patient was a man, 24 years old. Six years previously he had received a blow upon the head, and a few months later a tumor began to grow in that place. Six or eight similar tumors subsequently appeared on different parts of the scalp, and later these diminished in size. A large tumor situated over the left parietal regions and grew steadily until removed after about six months. Histologically, the tumor was found to be a fibrosarcoma.

Basal-Cell Epithelioma. A statistical study made by A. C. Broders' shows that this type of epithelioma occurs oftener in males than in females in the proportion of about 3 to 2.

1. The present series of cases represents 13.4 per cent. of 2,000 cases of general epithelioma.

2. Basal and squamous cells can be shown intimately connected in a neoplasm.

3. It seems to be a well-established fact that a basal-cell epithelioma can change into a squamous-cell epithelioma, or at least into an epithelioma in which the squamous cells predominate.

4. Basal cell epithelioma occurs oftener in males than in females, the proportion being about 3 to 2 in favor of the former.

The disease occurs in patients past middle life; with an average age of 56.7 years and oftener in farmers than in people of any other class. A family history of malignancy and a personal history of injury play a negligible part, but a previous mole, wart, pimple, eczema, scab, or ulcer, was associated in 37.1 per cent. of the cases.

The duration of the lesion shows a marked variation; it extends from three months to forty-five years, and averages seven years and one month. Ninety-six per cent. of all the lesions occurs above the clavicle. Thirty-six per cent. of all the patients had been either operated on or treated with acids or carbon dioxide snow before entering the Mayo Clinic. In approximately 75 per cent. of all the cases treated at the clinic there was either one excision with the knife alone or one excision with the knife immediately followed by cautery.

Of the 54.1 per cent. of patients heard from, 75.86 per cent. are living of whom 74.45 per cent. report a good result. In the cases in which a good result was reported, 74.68 per cent. of the patients had either one excision with the knife alone or one excision with the knife, immediately followed by cautery. The patients treated with acids or carbon dioxide snow, before entering the clinic did not get so good a result as those who had had no previous treatment.

The low grade of malignancy of the neoplasm is evidenced by its long duration, lack of metastasis in a single case in this series, response to proper surgical treatment, and by the fact that 75.45 per cent. of the patients reported living have been free from the disease on an

average of six years, one and six-tenths months. Of the patients reported dead, fewer than one-third died from this disease. Excessive exposure to sunlight as a cause of the neoplasm has not been borne out by the facts in this series of cases. It was noted that the hand, which is exposed to sunlight at least as much as any part of the body above the clavicles, did not show lesions.

Multiple Pigmented Idiopathic Sarcoma (Kaposi). Careful clinical histologic study of a case of multiple pigmented sarcoma was made by E. F. Skinner.⁸ The patient was a Jew tailor who noticed first in August, 1914, a lump about the size of a large pinhead, purple in color, and very itchy, on the back of the left hand. It remained quite small for four months and then began to get larger. In January, 1915, the left leg began to swell and an abscess developed on the external malleolus. This was opened by a physician and very soon afterward purple spots appeared on the left toes at the proximal ends. These spots gradually multiplied until they became very numerous on the left foot and leg. About the same time the right foot and leg became invaded by similar spots. In 1915, the man was treated by Sequeira with radiotherapy. Considerable improvement resulted and the patient was finally accepted by the army. Shortly after landing in France the spots recurred and he was invalided home.

When seen in 1918 there were lesions on the dorsal surfaces of the feet and of the left hand. The right hand remained unaffected. The patient complained of a great deal of pain at the site of the lesions, particularly in cold weather, at which time they occasionally became much darker. There was tenderness of the affected areas and sleep was disturbed by the pain in the toes. There was no history of syphilis and the Bordet-Wassermann reaction was negative. The study of the case by Skinner leads him to agree with the findings of MacLeod and others, that it is "not a sarcoma but a growth of organizing connective tissue cells, associated with marked vascular dilatation, edema and a deposition of blood pigment."

(8) Brit. Jour. Dermat., January, 1919.

Della Favera, on the other hand, regards the condition as a true sarcoma. He quotes Bernard, who states that Jews seem to be relatively frequent victims of the disease, which is opposed to the opinion of De Amicis who, although he had collected fifty cases himself, had never seen one in a Jew.

Radiotherapy seems to be the only remedy that has any effect and even that seems to be but temporary. Skinner believes that the cause of the inflammatory reaction is probably some circulatory toxin of very low virulence.

[We now have under observation a Jew aged 48 with multiple idiopathic sarcoma. He has made remarkable improvement under radiotherapy.—M.]

Method of Fixation of Paraffin Sections. A method for the fixation of paraffin sections to slides doing away with the troublesome albumin fixation is described by J. H. Mitchell.⁹ A small cotton swab which has been moistened in a 1 per cent. solution of acacia made slightly yellow by the addition of a few drops of 0.2 per cent. potassium bichromate, is rubbed lightly over a well-cleaned and flamed slide. No more than a mere trace of the fluid should be left on the slide. This is allowed to dry and the sections are floated upon the slide, then exposed to light for a few hours. No heating is necessary. The reaction depends upon the colloidal change taking place as the result of the action of the light. Care should be taken not to get too much of the fixative, or stained granules will be found in the sections.

MUCOUS MEMBRANE DISORDERS.

Cysts of the Labial Mucous Membrane. A search of the dermatologic literature by R. L. Sutton¹ failed to reveal any mention of this disorder, although it is rather frequently encountered.

Clinically, the simple retention cysts of the lip vary in size from that of a pinhead to that of a small hazelnut. the most common location is the lower lip at a point

(9) Jour. Amer. Med. Ass'n., Jan. 25, 1919.

(1) Jour. Cutan. Dis., December, 1919.

overlying the left cuspid tooth. The lesions are somewhat paler than the normal mucous membrane, and are painless. Frequently their presence is discovered through accident. When incised, a whitish, glairy, ropy fluid escapes. If the opening be allowed to close, the cyst promptly refills.

Of the eleven cases under the author's observation, nine occurred in men. In every instance the lower lip was the one involved.

Papillomata of the Buccal Mucous Membrane. Simple papillomata are found usually about the anus, the genital region and on the scalp. Papillomata of the mucous membrane of the mouth, however, are extremely rare. About the only mention of them in the literature is made by Brocq in his "*Traité élémentaire.*" Simon and Gastinel² describe papillomata occurring on the mucous membrane of the cheek along the line of the molar contact, and at the mucocutaneous junction of both the upper and lower lips. The lesions varied from opaline, flat neoplasms the size of a pinhead, and resembling verruca plana juvenilis, to sessile tumors. Interspersed with these tumors were typical and numerous lesions which were first described by Fordyce, and which are now known as Fordyce's disease.

Histologically, the tumors consisted essentially of a hyperplasia of the Malpighian layer, together with an increase in the corneous layer. There were numerous karyokinetic figures. The hyperacanthosis covered the markedly vascular prolongations of the tumors. In places perivascular infiltrations of plasma cells were found.

Papillomata of the Buccal Mucosa. A young Arab came under the observation of Levy-Bing and Gerbay³ for a primary lesion of the penis. Incidentally, they discovered in the mucous membrane of the right cheek a group of papillomata about 3 cm. in length, extending along the interdental line. Some of these were hemispherical and sessile, whereas others were much more voluminous, pedunculated and with mammillated summits. At the periphery of this principal mass were nu-

(2) Ann. de dermat. et de syph., December, 1919.

(3) Ann. des mal. vén., October, 1919.

merous small lesions varying in size from a scarcely visible elevation to a lesion the size of a pinhead. The color of the mucous membrane in this region was normal. The consistency was firm and supple and to the touch suggested the feeling of genital vegetations. The lesions had been present for about six months and had given the patient no concern, aside from the fact that in mastication they occasionally were bitten, and unusually hard food, like crusts of bread, irritated them.

TREATMENT OF DERMATOSES.

Symposium on Vaccine Therapy in Dermatology.

The editor of the *British Journal of Dermatology and Syphilis* invited a number of eminent British dermatologists to give their views concerning the value of vaccines as a curative agent. Of those responding to the request of the editor, Sequeira and Western⁴ seem to be the only men who retain the enthusiasm for vaccination which was the rule a few years ago. Adamson comes in for severe criticism by these authors for his attacks on vaccination.

Sequeira and Western believe that in active immunization whether by auto-inoculation or by the injection of an antigen, as in a vaccine, the first essential is that the lesion should be accessible to the body fluids. For instance, in a carbuncle or in a deeply-seated furuncle the lesion is in contact with the body fluids and with any immunizing substance circulating in these fluids. On the other hand, a pure acne lesion is anatomically outside the body, and is, therefore, inaccessible to immunizing substances in the circulation. It follows, therefore that the lesion which is well-bathed by body fluids is in a favorable position to stimulate the production of protective substances, and conversely the lesion which is practically outside the circulation affords no stimulus to the production of protective substances. The latter point applies equally to a lesion anatomically outside the circulation, as an acne comedo, and to an area of tissue cut off from the body fluids by fibrous-tissue for-

(4) Brit. Jour. Dermat. and Syph., April-June, 1919.

mation, which is always contracting. As a corollary to this it may be stated that the type of lesion for which assistance is most often required is the condition least favorable to vaccine therapy, and cases in which help can be given most advantageously are those in which such assistance is least often needed.

The stimulus, however, given by a lesion in contact with the circulating fluid in some cases fails (1) from over-stimulation and consequent paralysis of the local tissues, or (2) from under-stimulation to produce the necessary immunity. Here the introduction of a vaccine at some healthy part of the body may artificially stimulate the tissues to supply the required protective substances, which will then be carried to the lesion.

For instance, in a case of carbuncle in a man aged 70, the local tissue reaction failed, and an indolent condition resulted which lasted for a month in spite of repeated surgical interference. Granulation formation was entirely absent, the muscles being laid bare as if they had been dissected. After the administration of *Staphylococcus aureus* vaccine the cavity filled up by granulation and healed over rapidly.

A second principle which has a limited application in cutaneous disease, but is of a very high importance in surgical infections, is that dead tissue of any magnitude must be allowed an exit or be removed. The most common instances are those in which there is a caseous or broken-down tuberculous gland, or in which there is necrosed bone. In neither of these conditions can any striking or rapid improvement be expected from vaccine alone.

In staphylococcus infections the most striking successes are found in cases of deep-seated furuncle and carbuncle. This experience is in accord with that of other workers. They have been less fortunate in staphylococcus folliculitis, of which they have seen a large number of cases in soldiers. The lesions of streptococcus impetigo characterized by the formation of flat, epidermic vesicles containing serum, which rapidly dry up to form crusts, are usually so amenable to purely local measures that it is unnecessary to use vaccines. In erysipelas, however, striking results often follow the use of a suit-

able streptococcus vaccine. The rapid fall of temperature and abolition of the toxic condition are most marked. In mixed infections, the authors have occasionally seen remarkable benefit from vaccine therapy. Of tuberculous affections the writers have found that the dry type of lupus vulgaris does not respond to vaccine therapy, and this experience is entirely corroborated by that of Reyn in the Finsen Light Institute at Copenhagen. Here the explanation might appear to be that the protective substances do not reach the lesions but against this is the fact observed on several occasions by Sequeira that the development of acute tuberculosis has been followed by the rapid involution of areas of lupus vulgaris. In fact, the sudden rapid clearing up of a lupus area without obvious cause (such as intensive treatment) has come to be looked upon as a warning for careful examination of the lungs in the department for lupus at the London Hospital. The involution of the cutaneous disease in these cases must be due to the flooding of the tissues with protective substances developed in the pulmonary foci. It is not easy therefore, to explain why these cases of dry lupus should be so difficult to influence by the injection of tuberculin.

On the other hand, scrofuloderma and lupus of the ulcerative type have proved to be much more amenable to vaccine therapy. One case is cited of ulcerative lupus of the back of the hand in a boy, a condition which had involved the hand from the wrist to the metacarpophalangeal articulations and which had persisted for three years in spite of many varieties of dressing, x-rays, Finsen light, and curetting. The opsonic index to tubercle was found to be 0.3 and one injection of tuberculin was given. The whole area healed under fomentations in three weeks. The success was of short duration. The area broke down again and no benefit was derived from subsequent inoculations.

In tuberculides, they do not claim any practical results even when the dose of tuberculin (B. E.) was infinitesimal. Inasmuch as the most probable hypothesis explaining these conditions is that they are instances of Koch's phenomenon, *i. e.* the result of the inoculation with tuberculin of an individual already sensitised to tubercle,

one should not expect improvement by further inoculations. In this connection, the authors mention the fact that they have seen cold abscesses develop in the site of inoculation; lesions of the erythema nodosum type, develop at distant parts during a course of inoculation with B. E. in cases of tuberculosis of the lung, of the joints, and of the lymphatic glands.

In gonorrheal keratoderma remarkable improvement has been seen following the use of gonococcus vaccine. The carapace-like lesions on the soles have rapidly separated and the skin has speedily returned to a normal condition. Keratoderma blenorhagica is probably only encountered in cases in which the prostate is gravely infected by the gonococcus, and the bullae and keratosis of the plantar areas are due to toxic bodies developed in that organ. The protective substances developed by vaccines act directly upon this vascular organ and thus secondarily affect the cutaneous tissues of the soles.

The vaccine treatment of acne vulgaris is disappointing, yet in this disease vaccine therapy is more often practised than in any other skin affection. From the clinical point of view one must distinguish two distinct types of lesion—the comedo and the pustule. The comedo is essentially the product of a reaction of the lining of the pilosebaceous duct to *Bacillus acnes*. At this orifice the mass of acne bacilli is surrounded by epidermal cells derived from the lining of the duct. The invading organism is thus shut off from the circulation by this accumulation of epidermal cells. On the grounds already mentioned it does not seem likely that vaccines could influence the invading organism which is to all practical purposes outside the circulation, and therefore treatment by vaccines fails in this type of acne.

The occasionally brilliant results which have followed the administration of phylacogens are to be explained by the general reaction which occurs in some instances when these bodies are injected.

The Present Position of Curative Vaccination. Adamson⁵ attacks vaccine therapy in no uncertain terms. He reminds us that fifteen years ago Almroth Wright predicted that in future all microbial infections would

(5) Brit. Jour. Dermat. and Syph., April-June, 1919.

be dealt with by enhancing the resistance of the patient by means of vaccines rather than by attempting to kill the microörganisms by means of antiseptics. As everyone knows, the method of curative vaccination soon enjoyed an enormous popularity, so that some few years ago nearly every patient with a microbic infection, or with a supposed microbic infection, received some sort of vaccine treatment. But of recent years the vogue of vaccine treatment seems somewhat to have waned, and it is perhaps owing to the disappointment of this procedure that more attention has been of late devoted to chemico-therapy, or direct attempts to kill the microbes by the use of such drugs as arsenic, copper, manganese, tin and palladium.

Sir Almroth Wright himself appears to have modified his earlier opinion that "the principle of building up the resisting power of the system against any microbe which may have entered the body will ultimately hold its own even against the principle of warding off infection from the susceptible patient." For he has more recently said that "the prophylactic employment of vaccines is not only from the theoretical point of view the best of all methods of employing vaccines, but it is also the method which gives in practice the maximum advantage."

The value of prophylactic or preventive vaccination has been long firmly established; but the efficacy of vaccination as a curative agent is to-day still open to doubt. For many who have given this method a prolonged trial the results fail to satisfy their earlier expectations. It is probably true to say that many would hesitate at the present time before embarking a patient afflicted with sycosis or other chronic staphylococcus infection of the skin on a course of vaccine treatment, and that but few would now recommend vaccination by tuberculin as the best or even as a satisfactory method for the cure of lupus vulgaris.

Adamson's experience in the treatment of sycosis, of pustular acne, and of other chronic staphylococcus infections by vaccines has been distinctly disappointing, and he is unable to relate a single case of sycosis, acne, furunculosis or staphylococcus impetigo which has been

cured, or of which he could say that it has been definitely benefited by the treatment.

In recent cases of furunculosis the results have been somewhat more encouraging. In many of these more acute cases cures have resulted apparently as the result of vaccine treatment, although even here it is difficult to lay down any rules as to dosage, or to know beforehand whether vaccines are or are not likely to do good. In the treatment of lupus vulgaris by tuberculin, he has been altogether unfortunate, for although some cases have at first seemed to improve, there has been subsequently in nearly all a more rapid spread of the disease.

It is easy to attribute such unfavorable results to want of control by measurement of the opsonic index, to doses too large or too small or to use of vaccines not autogenous; but when we reflect, that, as regards staphylococcus infections, with the earlier and larger doses, cases were reported as doing well or as cured, and that these doses were regulated by the opsonic index; and that five years later, apparently as the result of clinical experience, the doses recommended were but one-twentieth of the earlier doses, we begin to doubt the value of the opsonic index as a guide. The fact that stock vaccines have been manufactured on a large scale and sold to the practitioner under the aegis of those who advocate this treatment makes one suppose that the use of autogenous vaccines is not regarded as essential.

The same may be said in respect of treatment of tuberculin. In the earlier days of the treatment, Sir Almroth Wright reported cases of lupus as doing well with doses of $1/500$ to $1/20$ mgm., of new tuberculin, the doses being controlled by the opsonic index. In 1910, the maximum dose recommended was $1/20,000$ to $1/4,000$ mgrm. This dose has not been confirmed as to the proper one and we have no indication as to the doses suitable for the cure of lupus vulgaris—a disease for which all dermatologists would like to know an efficient remedy.

How are we to account for this uncertainty of the results of curative vaccine treatment and for its failure to fulfill the early confident prophesy that it would supplant all the older methods of treatment? Is it not, perhaps, that the hypothesis upon which it is founded is

incorrect and does not afford therefore, a precise means for its use? Sir Almroth Wright's method is based on the hypotheses "that the blood of those who become the subject of a bacterial infection is deficient in protective substances," and "that by an injection of corresponding bacterial vaccines the content of the blood in protective substances can in practically all cases be increased." But this hypothesis seems to ignore altogether the teaching that an infected organism has already developed immune bodies as a consequence of becoming infected; that an animal which has become infected by a microörganism has been rendered super-sensitized to the toxins of that microörganism, or, to the use of the expression of von Pirquet, is in a state of allergy or altered activity towards that microörganism. We know, for example, that a patient who has not been infected by tuberculosis can tolerate a very much larger dose of tuberculin than can a patient who is already tuberculous. A minute dose of tuberculin given to a tuberculous patient may give rise to a reaction which is enormous in proportion to the dose. It is the omission to recognize this fact which seems to be the flaw in the method of curative vaccine treatment. We have no means of estimating the result of a vaccine in an already infected subject.

Sir Almroth Wright seems recently to have realized this flaw in the procedure of curative vaccination, for he says in a lecture "On the Lessons of the War," (*Lancet*, March 29, 1919,) that it has been accepted that to inoculate microbes into the already infected system would be as illogical as to instil further poison into an already poisoned system. He endeavors to justify his procedure of vaccination after infection under certain circumstances by assuming that in localized infections we have only localized responses, and that we may in such cases, therefore, make use of those regions of the body which are infected for the purposes of stimulating immunizing responses. But the assumption that in a localized infection the immunity response remains local is entirely opposed to known facts and to the teaching of immunology.

In conclusion, Adamson says that while it may be

admitted that strikingly good results do sometimes occur as the result of vaccine treatment, we have no precise means of knowing in what doses to use it in any particular case and no sound explanation for its action. Nor do we know why in the majority of cases it fails to effect a cure and only occasionally gives satisfactory results.

Vaccine Therapy in Diseases of the Skin. Whitfield⁶ says that, putting all figures aside, it is undoubtedly the fact that some cases have been so favorably influenced by the inoculation treatment that this favorable influence can not be dismissed lightly as a mere coincidence of the treatment with a spontaneously developing favorable turn in the disease. Also, admitting the previous statement to be true, many cases have shown no such favorable influence, and while only few may be said to have been definitely aggravated by the treatment, many seem to have been entirely unaltered. These two statements will meet with very little contradiction and and such contradiction comes from, first, the man who may be termed the professional inoculationist, and secondly the man who if he does not score an uninterrupted series of successes, will reject the treatment rather than work patiently to discover the cause of his failures.

The reason for the over-enthusiastic opinion of the former of these two men seems to be the unconscious desire to retain the patient within his sphere. "If this case is not suitable for inoculation it is not one for me to treat" necessitates the handing over of the patient to someone else, and a certain feeling of inferiority which ought not to be present.

The man in the second class is usually one with little or no knowledge of detail in dermatology, and one therefore who inoculates when at all in a somewhat haphazard manner without sufficient clinical investigation.

There is also, alas, a third class consisting of men who consider that if they have wiped a platinum loop over the affected area and produced a culture on some common medium they have thereby secured a vaccine containing the causal agent, and are in a position without further examination to treat the disease. In summing up, Whitfield says that in certain diseases, which usually

(6) Brit. Jour. Dermat. and Syph., April-June, 1919.

run a short course under what one may call ordinary treatment, the inoculation treatment often achieves brilliant results in the exceptional cases in which the disease proves resistant and tends to degenerate into a chronic malady.

In most cases of relapsing acute infections of the skin in which no constitutional defect and no exposure to local irritants (other than bacteria, of course) can be detected, the inoculation treatment very frequently interrupts and brings to an end the series of relapses.

In diseases of clearly chronic course, and especially in those in which the skin undergoes obvious structural change, inoculation has proved unavailing even though carried on in hospital patients for two years.

In dermatoses apparently dependent on infections of other parts of the body, but not themselves infective in nature there is some evidence that inoculation treatment of the infected organ aids in restoring to the skin its normal power of resisting adverse external influences.

The inoculation treatment does not absolve us from making as complete and thorough as possible an examination of the patient from all points of view. For this reason, the patient with skin trouble must be examined first by a competent dermatologist who should seek the aid of his medical colleagues and of pathologist in those cases in which the medical or pathologic investigations is beyond his technique.

Vaccines in Treatment of Cutaneous Diseases. Macleod and Topley⁷ state that of all the conditions which they have treated with vaccines, the only ones in which there has been definite and immediate benefit have been suppurating staphylococcus lesions, especially acute recent, and recurrent boils. By vaccines, both stock and autogenous, they have been able to cause the rapid involution of boils without the assistance of any form of local treatment, and in almost every case to keep the patient free from recurrences though there has often been a tendency to relapse after the cessation of the vaccine treatment. In the case of chronic boils, however, especially those about the back of the neck, the results have been more uncertain and sometimes unsatisfactory.

(7) Brit. Jour. Dermat. and Syph., April-June, 1919.

This is possibly due to the fact that acute boils are fairly well supplied with blood and the protective substances called forth by the vaccines have comparatively free access to the affected tissue, whereas in chronic boils, where there has been healing of certain lesions and the formation of a scar-tissue, the circulation through the boil is impeded. The initial dosage in these cases has been varied inversely with the severity of the general symptoms.

In several cases of bullous impetigo in children autogenous streptococcus vaccines were tried, but as these were combined with thorough local measures it was not possible to estimate their true value, and all that can be said is that they did not retard the cure.

In *acne vulgaris* the results, on the whole, have been unsatisfactory. In cases in which suppurating lesions predominated, benefit was derived from injections of staphylococcus vaccine or from a mixed staphylococcus and *acne bacillus* vaccine in so far as the diminution of the pustulation was concerned, but little impression was made on the comedones, and when the vaccines were discontinued an exacerbation of the pustulation generally took place—indeed, some of the worst cases of *acne vulgaris* seen were those in which vaccines had been used. The authors consider that vaccine forms no substitute for other methods of treatment in this disease and should only be resorted to under special conditions.

In those cases of *acne*—chiefly in adult women—in which the comedones are few or absent and which are associated with small, more or less indolent subcutaneous abscesses, the results from vaccines have been equally unsatisfactory.

In coccogenic sycosis the results have been uncertain and disappointing, and not to be compared with those obtained from *x-ray* treatment combined with suitable local applications.

The writers have tried the effect of the old tuberculin and of bacillary emulsion in the treatment of various forms of tuberculosis cutis, especially *lupus vulgaris* and *serofuloderma*. Improvement was obtained from Koch's original tuberculin in *lupus* in which superficially ulcerated patches were present and healing has taken place on the subsidence of the local reaction; but this pro-

cedure, even when small doses such as 0.25 c.c. of 1 in 1,000 were given, is too dangerous because of the possibility of stirring up unknown foci of tuberculosis in vital organs such as the lungs.

The results with bacillary emulsion have been very irregular, and though some improvement has been obtained at times in no case did the benefit from injections in any way compare with that which could be obtained from appropriate local treatment.

Chaulmoogra Oil in Treatment of Leprosy. Chaulmoogra oil has been the one remedy in the past decade that has stood the test of the clinical experiments and it is accepted by all that the internal use of chaulmoogra oil in large doses over more or less long periods of time will ameliorate the clinical manifestations of the disease in nearly all cases of leprosy.

During the past twelve years Hollman⁸ has seen cases in which the manifestations of the disease have disappeared and the lesions become bacteriologically negative from the internal administration of the oil alone. To obtain this result requires faithful administration of large doses over a period of many months, even years.

In 1904, Heiser published the results of the treatment of leprosy with the formula devised by Mercado; Chaulmoogra oil 60 c.c.; camphorated oil 60 c.c.; resorcin 4 gm. With the use of this preparation, five patients apparently recovered clinically, one of the five also being free of the bacilli. The publication of Heiser's report led to further studies in the hypodermic method of administering the oil. It is found on reviewing the literature on the subcutaneous administration of the oil that Tourtoulès of Cairo, as far back as 1899, used the oil hypodermically. Jeanselme in 1911, used a mixture of chaulmoogra oil, camphor and guaiacol. In 1916 McCoy and Hollman published the results obtained in treating cases of leprosy by the subcutaneous method. In sixteen cases under treatment from ten to seventeen months, ten were improved, four were stationary, and in two the disease advanced. In twenty-six cases the oil had not been administered long enough to permit publication of

(8) Jour. Cutan. Dis., June, 1919.

results. Late in 1916, Currie and Hollman devised the following formula for subcutaneous use:

	gm. or c.c.
Oil eucalyptus	8
Camphor	2
Iodine	1
Olive oil	147
Chaulmoogra oil.....	150

Mix in the order given—using heat. Maximum dose 10 c.c. intramuscularly, once a week.

Detailed histories are given of twelve cases treated hypodermically with these mixtures. Of the twelve cases of leprosy which became arrested under treatment, in two subsequently there was a recurrence of the disease, one within seven months and one within two years.

Fatty Acid Fractions from Chaulmoogra Oil. The results of the treatment of leprosy with sodium gynocardate, first used by Rogers, have been given in the Practical Medicine Series in 1917 and 1918. A. L. Dean,⁹ in an attempt to isolate the active principle from chaulmoogra oil, has prepared four fatty acid fractions which were tested therapeutically in the treatment of leprosy. The following are the four fractions:

A. Ethyl ester of chaulmoogric acid.

B. Ethyl esters of acids crystallizing from alcohol with chaulmoogric acid in the initial separation.

C. Ethyl esters of acids soluble in 92 per cent. alcohol in first separation and which form ether soluble lead salts.

D. Ethyl esters of acids forming lead salts insoluble in ether.

These fractions so-called A, B, C, and D with the exception of A, are not in a pure state; that is to say—fraction A is chaulmoogric acid ester; fraction B probably contains a small amount of chaulmoogric acid; fraction C probably contains a small quantity of fraction B; fraction D likewise contains a small quantity of fraction C.

Ethyl Ester of Chaulmoogric Acid in "Fraction A": A clear very fluid yellow liquid having the color of a heavy type of sauterne. When rubbed on the palms of

(9) Jour. Cutan. Dis., June, 1919.

the hands it emits a faint odor like that of chaulmoogra plus a sulphurous odor which is found present after ether has evaporated from a surface.

Ethly Ester "Fraction C": A medium heavy fluid of reddish brown appearance; deep brown in color when seen in a considerable quantity, but when shaken so as to smear the inner coating of the glass container with a thin fluid, possessing a reddish brown color identical in shade with the fluid extracts, of glycyrrhiza, having a faint odor of chaulmoogra oil.

Ethyl Esther "Fraction D": A medium heavy fluid of a brownish red appearance, deep red in color when seen in a considerable quantity, having a slight odor of chaulmoogra oil.

Preparation of the Acids for Hypodermic Use: The solutions were first heated on an electric hot plate for from 24 to 48 hours until no further odor of ether was present. They were then sterilized in the autoclave at 15 pounds pressure for one hour.

Dosage: The initial dose was 0.1 c.c. intramuscularly deep into the buttocks. The dose was increased 0.1 c.c. each week until 0.5 c.c. was given; it was then increased 0.5 c.c. at each treatment until the amount given caused a severe local reaction at the site of injection. This point varied in different patients and with the different fractions. *A* and *D* fractions caused the least disturbance, and the ethyl ester of the combined four fractions the greatest amount of local disturbance at the site of injection.

Toxicity: For animals—Guinea-pigs and rabbits were inoculated subcutaneously with 1 c.c. of each of the four fatty acid fractions with no harmful effect, except localized abscesses at site of each inoculation in fractions *A*, *B* and *C*.

Severe vertigo lasting about five minutes frequently followed the injection of over 2 c.c. of any of the four fractions. This was often followed by headache lasting from a few hours to a day.

Fractions *A* and *D* have caused the least amount of disturbance of any of the four fractions. Of the four patients who have received Fraction *C*, three have experienced severe cardiac depression following the injections.

In one case the severe vertigo was followed by unconsciousness, which lasted from three to five minutes. Extreme weakness accompanied by vertigo was experienced on attempting to rise from a recumbent position. The reaction was three days in passing off. In another case marked vertigo, with cardiac depression and weakness followed each 3 c. c. dose of this Fraction *C*.

Reactions: In the cases under treatment only one was of the pure nerve type. In this no reaction was observed. In all of the nodular cases there have been local reactions at the site of leprous lesions. They vary in severity from a hyperemia of existing lesions to a marked erysipelatous inflammatory reaction, which in two cases under observation lasted four weeks and was followed by marked pigmentation of the skin. One received *A*, and one *B* fraction.

In two other cases the reaction usually started at the site of lesions on the arms or legs, which became inflamed, painful and the skin tense. The area of inflammatory reaction extending around the lesion often measured from 6 to 8 cm. Both received *B* fraction.

In one advanced nodular case, with multiple small nodules scattered over nearly the entire skin surface, the reaction had been carefully watched. The nodules became inflamed and slightly swollen for a day or two. When this subsided there was a slight shrinkage in the size of the nodules. This continued after each injection until the nodule had been entirely absorbed, leaving a marked, crater-like depression covered by finely wrinkled skin. A biopsy of the site revealed no *B. leprae*. This patient received Fraction *D*.

While the indications are that Fraction *C* and Fraction *D* are more rapid in their actions than the other fractions, the number in the series of cases has been too small to say positively. The difficulty was insurmountable owing to the fact that the number of cases depended on the amount of the acid fractions Dean was able to isolate. Of the twenty-six patients treated over four months, all showed improvement and many showed very marked improvement. Eight of the twenty-six have already become bacteriologically negative and have been paroled from segregation.

Sodium Gynocardate Intravenously in Leprosy. In

the two preceding volumes of this series the results of the treatment of leprosy by the intravenous injection of sodium gynocardate, as first used by Rogers were recorded.

A very favorable report of the results obtained by the use of this method in thirty cases is made by Muir.¹ The author considers the therapeutic results to be far superior to those of any other drug or method of treatment. As a rule the most rapid progress was recorded in the youngest patients and in those cases of the shortest duration. This, however, is not always the case as the disease may advance more rapidly in some individuals than in others.

Sodium Gynocardate and Sodium Gynocardate "A" in Leprosy. Thirteen cases in a prison were treated by M. Carthew,² with sodium gynocardate intravenously and by the mouth in the manner described by Rogers. Later on they were treated with sodium gynocardate "A" intravenously and by the mouth inasmuch as the manufacture of sodium gynocardate had ceased. On a few occasions, and for short periods while the veins were blocked, the drug was injected subcutaneously.

Either one drug or the other had been administered practically continually, but on a few occasions the drug had to be stopped for a few days owing to reactions or some ordinary illness on the part of the patient, and also difficulty in obtaining the drug. In only one single case was there a severe reaction.

Of the thirteen patients, seven showed the symptoms of leprosy some time after being imprisoned, therefore it appears as if they were infected in the prison, especially as no method of isolation was employed and as the prison has contained lepers for many years past. Of the maculo-leprosy type there were nine cases and of mixed leprosy four cases. Classification of the therapeutic results obtained by this method of treatment follows: all lesions disappeared in two cases; very marked improvement in three cases; considerable improvement in six cases; improvement in one case; no improvement in one case. Neither the duration of the disease nor the

(1) Indian Med. Gaz., June, 1918.

(2) Ibid November, 1918.

type of the disease seems to have any marked influence on the rapidity of the improvement.

In the opinion of the writer, the relief granted to the patient by the improvement of this general health, together with the almost universal improvement of the symptoms of the disease, indicate that the treatment by sodium gynocardate A is indicated in all cases of leprosy of whatever type or duration. Although it is still too early to state definitely that the treatment is specific and curative, the results already obtained strongly indicate that happy result.

Local Application of Arsphenamin in Vincent's Angina. The value of the local application of arsphenamine in the fuso-spirillum infection of the mucous membranes has been frequently reported. Some authors have maintained that intravenous use of arsphenamin would give the same results. This, however, is now found not to be the case. Gougerot, Goullier and Vaslin³ report the case of a young soldier who had a fuso-spirillum infection of the tongue which was first supposed to be syphilitic, and for which intravenous arsphenamin treatment was administered. The lesions were somewhat lessened in their extent and severity, but after about twelve days recurred, leading to superficial ulceration of the tongue. When seen by the authors, the ulcer closely resembled syphilitic ulceration, but it had more of a pseudo-membranous aspect, and the odor of the breath, together with the painful deglutition and the submaxillary adenitis, led them to suspect Vincent's angina. In order to demonstrate that it was not syphilis, intravenous injections were continued and several Bordet-Wassermann tests were made, all of which were negative. There was no improvement and it was then decided to apply neo-arsphenamin locally. After eight days of local applications the progress ceased and in twelve days there was complete healing. The case is interesting in that it showed the close resemblance of Vincent's angina to gummatous syphilitic lesions of the tongue, of which there was even a marked infiltration. Moreover, it showed the inefficacy of two series of intra-

(3) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

venous injections of arsphenamin and the rapid results obtained by using the local applications of this drug.

Another case of similar ulceration of the tongue with marked induration is reported by Schulmann and Thibaut.⁴ The patient was a soldier, 22 years old, who had had the condition of the tongue for two weeks, when first seen by the authors. On the left side of the tongue there was an ulceration, varying in depth, with marked induration beneath. The patient was scarcely able to move his tongue in speaking or in deglutition. He had been evacuated from the front to the dermatologic center with the diagnosis of syphilis. The Bordet-Wassermann test was negative and under hydrogen peroxide lavage prompt healing occurred.

Treatment of Erysipelas with Antistreptococcus Serum. A series of eighty cases of erysipelas were treated with a polyvalent antistreptococcus serum by W. H. Guy⁵ at Camp Travis, Texas. The serum was used in all cases, and many patients received no other treatment. After observation and comparison of the results of various local applications the author is of the opinion that they have but little influence in limiting the spread of the infection and, therefore, may be dispensed with.

By the use of the polyvalent streptococcus serum, 75 per cent. of the cases were favorably influenced. Amelioration of symptoms was too closely connected with the administration of serum to be explained on any other basis. An abortive effect was obtained in two cases which were injected within the first six hours of the infection. In the majority of cases following the administration of serum there was a fall in temperature, pulse rate and respiration, followed in the course of a few hours by a slowly mounting temperature, which, however, usually did not reach its original height. At the same time, the toxemia was lessened and patients were comparatively comfortable. Second and third injections usually acted in the same way, with the result that the course of the disease was in many cases probably shortened, and in most cases certainly modified as to severity. In about 25 per cent. of the cases the serum seemed to have abso-

(4) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(5) Jour. Cutan. Dis., June, 1919.

lutely no effect, and in the majority of the cases forming this 25 per cent. no particular reason could be assigned for this failure of therapy, but two cases were probably accounted for by reason of general debility.

Theorizing, one might consider the possibility of an unusually severe infection or the presence of an unusual strain of streptococcus not antagonized by the antiserum. It was noteworthy in this series that the earlier the serum was given, the better the result. The first few injections were given subcutaneously with rather indifferent results and later the intravenous method was adopted. This has the advantage of being almost painless, and the clinical response to serum given in this manner is greater. About 2 c.c. were given subcutaneously as a desensitizing dose and an hour later 20 c. c. were given intravenously. In highly toxic cases it was found to be advantageous to give from 40 to 100 c.c. for the first injection, but in the majority of cases 20 c.c. doses were sufficient.

There was no fatality in the series. The average febrile period was nine and one-half days. Transient albuminuria was seen several times, but two cases showed albumin with granular casts. Cardiac complications were not seen—two doubtful cases were ruled out by the chief of the medical service. Abscess developed in one case. Suppurate otitis media was seen twice as a complication. Second attacks developed in three instances.

Whether the therapeutic action of antistreptococcus serum is due to its specific antistreptococcus properties or merely the result of the introduction of so much foreign protein, the writer is unable to state, but he feels that it is a valuable aid in the treatment of erysipelas.

Picric-Brass Preparations in Treatment of Lupus.

A revival in interest of the use of copper in the treatment of lupus vulgaris has been brought about by the work of H. A. Ellis.⁶ The preparation first used by the author approximated an old formula for making brass. It is formed by combining basic copper sulphate with basic zinc sulphate in the proportion of 86 per cent. basic copper to 14 per cent. basic zinc. The basis of

(6) Lancet, March 15, 1919.

the preparation has been used by Ellis for many years in intractable chronic eczema, nearly always with success. It had considerable restrictions in lupus, but a continuous series of experiments has gradually eliminated them. This paste is easy to apply. When the covering plaster is removed after forty-eight hours the tuberculous tissue will be found extensively destroyed and removable as small caseating nodules, while the uninfected tissue is uninjured. The caseous material is often stained with the preparation, but the healthy tissue is not. This localized destruction gives a curious and characteristic appearance, especially in tuberculosis *verrucosa cutis*. Where the tuberculosis deposit is superficial and limited, comparatively few applications destroy the growth, but in the majority of cases many applications are necessary. The problem is only one of contact; if contact can be obtained the result is always assured.

The paste is quite innocuous to healthy tissue, and can be placed in the eye without causing other than temporary irritation which is easily controlled by first instilling eucaïne and adrenalin. This is shown in the case of a patient cured by the application of the paste to the conjunctiva of the everted eyelid, resulting in removal of all tuberculous tissue. The paste can also be applied to the nasal mucous membrane without producing any reaction unless the tissue is invaded by tubercles. But if the nasal mucous membrane be involved caution must be used or it is apt to produce headaches, which may be very serious if the nasal fossae are involved. Ordinary non-tuberculous ulcerated surfaces are not affected by the application, and it has apparently little effect on their progress.

In their earlier investigations, as has been so frequently the case with lupus, the results were unequal; and certain disadvantages delayed the publication of the method. The most serious and difficult was a tendency to light up some quiescent focus. These manifestations were sometimes accompanied by certain constitutional results. This disadvantage has now been remedied by the addition of trinitrophenyl.

It was at first difficult or impossible to reach the deeper deposits. Then there were also the various thick-

enings of the cutaneous and other tissues of a lymphatic or glandular nature so intimately associated with tuberculous lesions, which were uninfluenced by the earlier preparations. The superficial tuberculous abscess presented certain problems, all its own, especially the cold, small, non-spreading tuberculous abscess formation limited to the skin entirely, which is not usually accompanied by glandular enlargement. It is often multiple, and this condition, for purposes of differentiation, Ellis calls intradermic abscess, as a distinct division of lupus.

These abscesses are surrounded by healthy tissue, and there is little or no tendency to invade the adjacent area. They are very difficult to heal and leave many of the unsightly scars. They are placed under the head of scrofuloderma, but the absence of glandular enlargement precludes that term. They are invariably tuberculous, and the majority up to the present have been due to the bovine bacillus.

For these conditions a suitable medium is a fluid preparation called brass' oil, or shortly "bro." Its extensive and general application has produced many unexpectedly favorable results. This oil, transparent and green in color, is produced at a definite temperature, over a considerable period, and is applied on gauze, covered with jaconet and left for from two to seven days. Definite constitutional symptoms indicate that it is partly absorbed along the line of the lymphatics, though these may largely be due to the resolution and absorption of the tuberculous materials. The conditions which yield most readily to its influence are those produced by lymphatic thickening, especially the condition constituting pseudo-elephantiasis, as well as the general thickening in scrofuloderma. The swellings in the neighborhood of joint or bone disease are also reduced by it; in fact, all swellings produced by lymphatic obstructions, the result of tuberculous invasion. It was the early investigation of the "bro" treatment that brought most into prominence the lighting up of distant foci and the constitutional disturbances.

On further investigation, it was found that the trinitrophenyl or picric series had a distinct action in controlling these conditions, and extended observations—not yet completed—resulted in a further addition of a

definite proportion of trinitrophenyl to the brass preparations. After this addition, metastatic developments entirely ceased, and cases of pallor and loss of weight no longer occurred, but distinct improvement of the general appearance and health. The specific action of the brass treatment was materially increased, and unlooked-for and very gratifying attainment.

In certain individuals, however, a superficial dermatitis limited the use of the new remedy, although the condition was very rapidly relieved by soda-bicarbonate solution. No effect is exerted on the deeper tissues, as was seen when "trino" or picric "bro" was injected into abscesses or sinuses.

One of the means of testing the efficiency of the remedy is as follows: When a smear of caseous material from a tuberculous deposit is made on ordinary Dorset egg medium, a slight guttering is often produced due to its solution. This is probably due to the action of trypsin or some other ferment released by the process of caseation. This guttering did not occur when the brass media were mixed with the pus of ordinary abscesses. Accurate determination has yet to be made, but it has proved a good rough-and-ready method of testing the efficiency of the various products during the search for increased efficiency, and when compared with the tissue destruction effect proved fairly reliable.

By using these preparations, it was easy to obtain pure cultures of the particular organism causing the disease, proving also that the remedy was not immediately destructive to the life of the bacillus, but a series of observations showed the gradual breaking up of the organism.

At the present time, there are available four preparations of specific potency in tuberculous deposits. These preparations are: (1) Brass paste, an oily preparation of a compound of basic sulphate of zinc and copper; (2) brass oil or "bro," a preparation of the soluble portions; (3) and (4) both these preparations, in combination with approximately 1 per cent. of trinitrophenyl, called respectively "trino-brass" and "trino-bro." Great care is needed in preparation as they are easily decomposed and rendered inert at comparatively low temperature. Instability is naturally a condition, for if

the combinations were not weakly allied they presumably would not obtain their specific action. These preparations are more efficient, especially in facial cases, when mixed with adrenalin and cocaine or eucaine.

The application of the brass paste is made every two or three days under zinc plaster. The "bro" is applied either as a foment on gauze with jaconet covering once, twice, or thrice weekly, as indicated, or only painted on the skin when a rest from active treatment is required. The "bro" collar is the most efficient way of dealing with glands of the neck or scrofuloderma; it very rapidly diminishes the lymphatic engorgement, and is applied twice weekly and should cover all round the neck from ear to collar bone. The staining of the skin is easily removed with vaseline. The "trino-bro" is the best preparation for these cases unless they are picric sensitives, which are rare.

Antimony in the Treatment of American Leishmaniasis of the Skin. The intravenous injection of antimony tartrate in Leishmaniasis of the skin has been referred to in these volumes in the past two years.

Cases of American dermal leishmaniasis are not commonly seen in England, and the case recorded by G. C. Low⁷ is of special interest because of its long duration and because no secondary buccal lesion developed, a contingency always to be dreaded.

The patient in the case reported was born in Scotland, and served in the Indian army for thirty-three years (1876-1909). After leaving India he went to Portuguese West Africa for a trip; in 1909 and again in 1910 he visited Central America, traveling on the frontiers of Guatemala and British Honduras. He returned to England in July, 1910, and remained until October, 1910, when he went to Portugal. Since that date he has been in Portugal for the greater part of every year until 1917; he visited San Thome for a trip in 1912. From 1917 to the present date he has lived in London.

In October, 1910, when in England he noticed a horny oval yellowish scale, $\frac{1}{2}$ in. on the pinna of the right ear. He picked it off, leaving an open sore which showed no signs of healing. In January, 1911, he suf-

(7) Brit. Med. Jour., April, 1919.

ferred from influenza followed by pneumonia, and at this time the sore became larger. Mercurial ointments were then tried, but did no good. Although the Bordet-Wassermann test gave negative results in 1912, he took a course of mercury and potassium iodide spread over a period of five months with no result, the sore continuing to perforate the ear till it formed a complete passage, when it continued to spread round the edges. In 1911 when in Portugal for the winter, the sore became much worse and the lower part of the ear became very much swollen. The condition was then diagnosed as malignant disease, rodent ulcer, and syphilis by different observers.

When seen by the author about an inch of the pinna of the right ear was gone; the area was dry except at the top, and also at the lower margin and there were signs that the disease still existed and was spreading. The part was tender and red.

The tartar emetic was dissolved in 2 oz. of normal saline, sterilized, and run into the vein at body temperature. Twenty-eight injections were given in a period of a little more than three months. The dose at first was $1\frac{1}{2}$ grain which was gradually increased until $2\frac{1}{2}$ grains were given.

The effect upon the lesion was striking; a very distinct improvement was noticeable after the fifth injection. For all practical purposes the ear was cured after the twentieth injection, but to make certain the injections were carried on for another month, a total of 47 grains in all having then been given.

Treatment of Multiple Warts. Stelwagen has recommended use of a saturated solution of salicylic acid in alcohol for the treatment of verruca plana juvenilis, but this alone is not of much value. Charles Ind^s has supplemented this preparation by shaving off the growths with a sharp blade bevelled only on one side. The warts and skin around are painted three times a day for one day with the salicylic acid liquid. On the following morning, they are cut off by the knife; this passes freely over the healthy skin, but when it comes to the wart cuts it off, leaving a slightly bleeding point. The surface is

painted at once with the salicylic solution and twice more later during the same day, three times in all. This turns the little red points to a brownish-black color, tiny scabs form which are allowed to drop off, taking about a week to do so, and leaving a perfectly clear healthy skin. The forehead is bathed with pure alcohol once a day until the scabs have all dropped off.

A razor is of no use; a sharp flat instrument pushed over the skin is necessary. With this method there is neither pain nor scarring. The treatment is useless for larger warts.

Roentgen-Ray Treatment of Trichophytosis Capitis. Ringworm of the scalp is a very common disease among children. The statistics of the American Dermatological Association show that it constitutes over 3 per cent. of all dermatoses. The figures of Hazen show that it is three times as common in negroes as in whites. Why the disease should disappear spontaneously at puberty is a question that merits further study. Inasmuch as there are always marked changes taking place in the pilosebaceous structures during the adolescent period, it is not unlikely that as a result of these changes the soil is rendered unfavorable for the continued growth of these organisms.

The use of local applications in the treatment of ringworm of the scalp is highly unsatisfactory. Vaccines are of no value. Hand epilation is too slow, tedious, difficult and painful to be of value except when the infection occurs in one small area. Complete epilation is easily obtained by the use of the x-ray and the technique is well-described by Hazen.⁹

The technique used by Hazen was that advocated by MacKee and Remer.¹

It is not necessary that every hair in the head be removed; the falling of the diseased hairs and of the majority of the others is sufficient to effect a cure provided that the scalp be kept covered with an antiparasitic preparation.

Where there are but two or three small spots it is not necessary to treat the entire scalp if the child is subject to careful and intelligent supervision, but in the majority

(9) Jour. Cutan. Dis., May, 1919.

(1) Practical Medicine Series, 1915, Vol. IX.

of instances it is better to remove all of the hair at one sitting, for the falling hairs are almost certain to infect other portions of the scalp. If it be decided to treat will fit this spot and keep it adhering to the hair or else replace it as soon as it comes off. The hair will come off with the adhesive and not be scattered. Ordinarily, the defluvium is complete in about three weeks and the new hair returns in from six to twelve weeks after falling.

A mild antiseptic ointment must be used steadily until the scalp is clean. Yellow oxide of mercury in the strength of 12 grains to the ounce, or salicylic acid in the strength of from 15 to 20 grains to the ounce may be used. Under no circumstances must a sufficiently strong ointment be applied to cause an erythema, for this may cause permanent baldness. After the hair has but one spot, it is best to cut a piece of adhesive that fallen, full strength of practically any of the antiseptic ointments may be used to clear up any remaining patches.

To date the author has treated 225 cases of tinea tonsurans by this method. In seventeen instances but a portion of the scalp was epilated, and in fourteen of these it was later found necessary to remove all of the hair inasmuch as other patches of the disease developed. In one private case the mother refused to have the whole scalp epilated, and thirty-four different treatments were given to various sized patches before final recovery took place. In only one instance was there a recurrence, although there were six cases of new infection. In the one case of recurrence the hair was again epilated exactly three months from the date of the original treatment, with perfect results. The hair does not always return the same color. In a private patient with beautiful red hair the new hair was brown. At times the texture of the new hair is not the same as that of the old, an additional argument against partial epilation.

Radiotherapy in Extensive Dermatoses. In a paper read before the Section on Dermatology of the American Medical Association at Atlantic City, Wise² gives

(2) Jour. Amer. Med. Ass'n., Nov. 15, 1919.

his technique for the measurement of dosage and for the treatment of cutaneous lesions.

The apparatus used has been standardized according to the method suggested by MacKee and Remer. To obtain one Holzknacht unit at "skin distance," that is, with the exposed pastil of barium platinocyanide resting on the skin, the following factors were found to be serviceable as convenient working constants: length of parallel spark gap, 6 inches; amount of current passing through the tube, 2 milliamperes; distance from the anode to the skin, 8 inches; time of exposure, three minutes.

With the Coolidge tube backing up a 6-inch parallel spark gap, the Benoist penetrometer reading is approximately No. 8, that is, a "hard" ray. Experience has taught that a No. 8 to 9 *B* ray is to be preferred in dermatologic practice, to much softer or much harder emanations.

A stout wooden table, 6 1/2 feet long, 2 feet wide and of the height of an ordinary dining-room table, fitted with heavy roller casters, is most useful. It should be fitted with an adjustable head rest and leg and arm rests, preferably made of wood, and so constructed that they may be folded and put out of the way when not in use. A heavy tube stand, constructed with a well-balanced counterweight and a stout lead glass bowl for the Coolidge tube is to be preferred to the lighter wooden stands, because the risk of accident to tube and patient is thereby lessened with the use of a heavy apparatus. An overhead trolley system for conducting the leads to the tube, and a lead screen to protect the operator, complete the outfit.

In a general way, it may be said that the treatment of widespread and generalized skin diseases consists in the administration of repeated fractional doses to the entire affected integument. In the majority of eruptions a dose of one-eighth to one-quarter Holzknacht units at "skin distance," administered once or twice a week, over periods varying from two to eight weeks, is sufficient to bring about involution of many of the dermatoses amenable to the treatment, so that the skin is exposed to a total dosage varying from three-quarters to one

and a half Holz knecht units (skin distance) in from three to eight or nine weeks.

When large areas, such as the anterior surface of the trunk, or the entire back, are to be treated, the rays are so administered as to permit of an approximately equal distribution of the dose over the flat and convex surfaces of the body. This is accomplished by allowing the rays to overlap from different focal points of the tube, on the same principle as the Kienbock-Adamson method of treating ringworm of the scalp, although the accuracy of the latter method can not be duplicated in treating the trunk, nor is such exact dosage strictly necessary for practical purposes. The usual procedure is to expose certain regions of the skin in succession, as both sides of the upper chest, both sides of the midthoracic region and both sides of the abdominal region, each area receiving the required one-eighth to one-quarter unit of radiation.

It is unwise, and may even prove to be dangerous, to expose more than one-third or even one-fourth of the body surface at the same sitting, or on the same day. It is best to allow several days to intervene between the treatments, so that approximately two exposures a week are administered, when the entire skin requires radiation, the different regions of the body being treated at different times.

When treating extensive surfaces, such as the chest and abdomen or the back, cognizance must be taken of the law that the intensity varies inversely as the square of the distance. That is, the quantity of Roentgen rays striking a given area of integument varies inversely as the square of the distance between the anode and the skin. In the application of this rule in practice—for example, in exposing the entire chest of a man—the anode may be focused at a given distance above each nipple, to which areas a certain dose is administered, say one-fourth H unit over each breast. In this procedure, calculations based on the law of intensity determine the quantity of rays striking the area of skin between the two focal points, in this case, each nipple; that is to say, the sternal portion of the chest receives overlapping rays from each lateral exposure, approximately equivalent to one-eighth H unit from each side, resulting in a one-fourth H dose to the intermammary region.

VENEREAL DISEASES.

GONORRHEA.

EXPERIMENTAL STUDIES.

Experimental Gonococcus Infection in Animals.

From a search of the literature on this subject Culver¹ concludes that gonococcus infection in animals, in the sense that the organisms increase within the animals and invade their tissues, does not occur. The slight early increase in the number of organisms is explained apparently by the development on the artificial culture medium injected with the organisms, together with the lowered body temperature immediately following such an inoculation. The many positive reports are due to lesions produced by the injection of gonococcus toxin and not the result of gonococcus infection. The variability of reported results undoubtedly is due to the difference in virulence and toxin production of the various strains of gonococci as well as to the varied susceptibility of different animals of the same or different species and to the great change in the immunity of a single animal during the different seasons of the year.

The experimental work carried out by Culver shows that rabbit serum has a marked bactericidal action on gonococcus cultures. The titer varies for different rabbits but averages approximately 1/75. Gonococci readily adapt themselves to such bactericidal substances and by growing them on gradually increasing strengths of fresh rabbit serum broth, gonococci will readily grow on serum broth 1-2. One strain of gonococci adapted itself to whole rabbit serum in which it grew readily.

Successive transplantation of gonococci on rabbit blood agar increases the tolerance of these organisms for rabbit serum up to the twenty-sixth transfer. Further

(1) Jour. Urology, October, 1918.

transplantation neither increases nor decreases the tolerance already acquired. This serum fastness of gonococci seems highly persistent since it took twenty-five successive transplants on human blood agar to cause its complete disappearance. The serum-fast gonococci remain longer in the blood-stream of a rabbit than an ordinary strain of gonococci. Positive blood-cultures were obtained forty-eight hours after intravenous injection on three occasions and in one animal five days after injection. Ordinary gonococci do not so behave.

Positive blood-cultures were not obtained after intraperitoneal injections of gonococci. The organisms could usually be recovered from the peritoneal cavity up to twenty-four hours but rarely later.

There is no conclusive proof of gonococcus infection having taken place in any of the one hundred and thirty-two rabbits injected. Typical iritis developed in one animal twenty-four hours after intravenous injection. Gonococcus-like organisms were recovered but not completely identified. This lesion could not be reproduced by exactly similar methods.

UNUSUAL MANIFESTATIONS.

Verrucous and Papillomatous Genital Lesions in Gonorrhea. Verrucous and papillomatous lesions which are said by the authors, Gougerot and Clara,² to differ from the keratosis blenorrhagic of Jacquet-Chauffard, and from the lichenifications described by Brocq, have been observed in a number of cases of blenorrhagia.

The lesions are verrucous thickenings of a dirty-gray color(or black in the negro) with a flat surface which is somewhat villous, but the villi do not exceed 1 mm. in length. The borders are either sharply demarcated or "progressive" in which case the verrucous lesions gradually fade into the normal skin. The lesion is either in the form of small papules measuring from 2 to 6 mm. or else in diffuse plaques several centimeters in diameter. The lesions are found principally on the glans but occur also on the shaft of the penis, scrotum, inner surfaces of the thigh and even on the abdomen.

(2) Ann. des mal. vén., March, 1919.

In the opinion of the authors, the lesion is an epidermitis due to the gonococcus, and comparable to the epidermitis described by Gougerot (*Progrès Médical*, 1912) resulting from streptococcus infection.

Gonorrhea of an Epidermal Canal of the Raphe of the Penis. An interesting case of a canaliculus along the raphe of the penis which had become infected secondarily from a gonorrheal urethritis is reported by Milian.* The canal was removed surgically in its entirety. The wound suppurated for about two weeks and then cicatrized uneventfully. The canal was then examined histologically and found to consist of an infolding of epithelium which was exactly analogous to that of the skin in general and of the prepuce in particular. The greatest involvement of the canal by the inflammatory process was in the distal end in the region of the prepuce and was typical of urethral gonorrhea.

According to the author, the formation of this canal was a teratologic process in which the urogenital canal had, in closing, formed an invagination. The author had made no bibliographical researches, but in the discussion which followed the presentation of his paper it was brought out that Balzer and Druelle had reported similar observations but in these cases the canaliculi had been much shorter.

VACCINE THERAPY.

Pus Vaccines in Gonorrhea. The idea of making gonorrhea pus vaccine was suggested to E. G. D. Pineo and D. M. Baillie⁴ by Captain J. L. Lickley R. A. M. C., and a trial was made of a vaccine made from the pus of five cases. The results in gonorrheal rheumatism and epididymitis were encouraging, and a vaccine was next made from twenty-one acute cases; in each a preliminary microscopic examination was done for density and purity of growth. About 1 c.cm. of pus was pipetted from the urethra of each case and mixed with 10 c.cm. of 0.5 per cent. carbolized normal saline in a sterile test-tube. The twenty-one emulsions were transferred to a 500 c.cm.

(3) Bull. Soc. franc. de dermat. et de syph., 1919, No. 1.

(4) Lancet, March 29, 1919.

flask and well shaken. Glacial acetic acid in the proportion of 0.5 per cent. solution was added to dissolve the pus cells, a rubber cap put on and the whole shaken well for one hour. The emulsion was then diluted by equal part of 0.5 per cent. carbolized normal saline, making acetic acid 0.25 per cent., and put aside for four days to allow the phenol to kill off gonococci. The emulsion, counted against blood cells, was found to contain approximately 600 million per c.cm. It was tested aërobically and anaërobically for sterility, and finally diluted with 0.5 per cent. carbolized normal saline and put up in 50 c.cm. vaccine bottles. This resulted in a mixture containing approximately 24 millions of gonococci per cubic centimeter.

The advantages claimed are:

1. Ease and simplicity of manufacture.
2. High degree of polyvalency. The patients selected were infected in England, Scotland, Ireland, and France—in places as widely apart as Aberdeen, Belfast, Bristol, Hull, London, Paris, and Poperinghe. Torrey has shown by cross-agglutination and agglutinin absorption experiments that gonococci fall into about fourteen groups.
3. The high degree of virulence. The organisms have not been vitiated by growing on artificial media, but are fresh and virulent.

For chronic cases this vaccine was combined with the emulsion of ten strains of Gram-positive diphtheroid bacilli and of seven strains of *S. albus* isolated from chronic cases. The minimum doses of these were 60 million and 240 million respectively. The vaccine, plus diphtheroids, seemed to be more efficacious in gleet than G. C. alone.

There was an almost entire absence of the so-called "negative phase," even though doses were given every three days. Possibly the gonococci were to some extent sensitized in the body before discharge.

While recognizing that other workers have not always had similar results, the authors report the following as the chief points of experience gained:—

- a. No improvement can be expected and possibly harm may be done, by giving vaccines in the acute stage, except when the infection has become generalized—viz.,

in gonorrheal multiple arthritis, endocarditis and pericarditis.

b. The vaccine treatment of gonorrhea differs from other diseases in the possible production of a prolonged negative stage if too large a dose be given. The avoidance of this prolonged negative phase is the key to the successful use of a vaccine in gonorrhea. If the negative stage develop it is generally several weeks, sometimes months, before improvement is brought about. The indications of over-dosage are: (1) Local:—increased urethral discharge with increase of pus cells; increase of extracellular gonococci not due to a breakdown of purulent folliculitis. (2) General:—increased evening temperature (any temperature over 99° F. should be regarded as dangerous), malaise, headache. An evening temperature even of 99° F. for more than one night should be regarded as an indication of an overdose. Of these two indications the local is regarded as the more serious.

To avoid these dangerous effects it is necessary to commence with very small doses and gradually increase the dosage. The doses are much smaller than those used by many other workers—and also smaller than the authors formerly used—but experience of several thousands of cases treated with vaccines, in acute or chronic stage, has convinced them that these doses give the best results with the least number of relapses. Possibly the use of sensitized vaccines would obviate the dangerous “negative phase.”

The type of cases most benefited by vaccines are: (a) Chronic gleet stage coming on from about twenty to twenty-five days after commencement of discharge, with gonococci, intracellular and extra-cellular, in the discharge; (b) relapses generally stirred into activity by recent and repeated sexual connections, and drinking bouts; (c) gonorrheal rheumatism in acute or chronic stage; (d) gonorrheal ophthalmia, either metastatic or local infection type; (e) the rare cases of gonorrheal septicemia.

About 3,000 doses have altogether been given of this vaccine, and of these five cases had rises of temperature of about 99° F., on the evening following injection, and

one on three occasions. All the patients had normal temperatures next morning and remained so. All injections were given into the muscles of the arm or forearm (not subcutaneously). There was no pain and no local inflammation. All injections were given with usual aseptic precautions.

Detoxicated Vaccines in the Treatment of Gonorrhea.

The results of treatment with detoxicated gonococcus vaccines of a series of cases are set forth by David Lees.⁵ The vaccine is an adjunct to the local treatment which should be continued as usual. The amount of "anti-body" produced by the intramuscular injections of the detoxicated vaccine prepared after the manner of Thomson was controlled by complement-fixation tests at weekly intervals.

Detoxicated vaccine is practically non-toxic and in large doses very rarely causes a severe general reaction. It acts directly on the tissues and not by protein shock.

Even in doses of 2,500 millions up to 10,000 millions no such thing as a negative phase was produced. No other form of vaccine sensitized or otherwise prepared, and no phylacogen produces such rapid and great specific reactions unless used in toxic doses.

All vaccine-treated cases run a much milder course, and there is an absence of complications and less tendency to relapse, due to the fact that the patient has circulating in his blood for several months after the symptoms have disappeared sufficient antistubstance to protect him for some considerable time.

Removal of the toxic substance from vaccines opens up an immense field for the prophylactic and curative use of them in all diseases due to microorganisms. During the recent influenza epidemic Lees used detoxicated influenza vaccine and a compound detoxicated catarrh vaccine, with so far promising results, both as a prophylactic and as a cure. When secondary organisms are found in the urethral discharge it is advisable to use, in addition to gonococcus vaccine, one made up from the microorganisms found present. Detoxicated gonococcus vaccine should be of incalculable value in the complica-

(5) Lancet, June 28, 1919.

tions of gonorrhea in the female where local treatment is so limited.

Provocative Vaccine in Determining the Cure of Gonorrhea. One of the most difficult problems encountered in the management of a case of gonorrhea is to determine when the case is cured. Not only is this important from the standpoint of the patient himself but the evils which follow in the wake of an uncured case, discharged as cured and affecting innocent persons, make the question a vital one. The absence of clinical signs, *i. e.*, the disappearance of the discharge and the filaments in the urine does not prove necessarily that a cure has taken place, for this evidence is frequently falsified by the recurrence of the discharge, crowded with gonococci, when no fresh exposure has occurred.

For some time it has been known that an injection of a gonococcus vaccine has an effect in altering the clinical symptoms. Following such an injection the added endotoxin is too much for the defensive immunity produced by the body against the original infection so that, for the time being, the defenses are overwhelmed. Resistance is lowered and the gonococcus is enabled to proliferate in peace. This negative phase lasts from forty-eight to seventy-two hours and is followed by a positive phase in which the defences of the body are stimulated and produce sufficient antibodies to neutralize the added toxin plus the toxin absorbed from the original infection. During the negative phase should any gonococci be hidden in the depth of the tissue they will grow and probably break through to the surface of the mucous membrane.

Any condition tending to lower the specific bodily resistance may cause a relapse of the disease. To produce this a single injection of a potent gonococcus vaccine has been recommended by several observers, notably McDonagh and Asch. These facts led G. H. Pearson⁶ to use two doses on successive mornings as a test of cure. In no cases did the vaccine produce a general reaction nor was any discomfort caused to the patient and no complications followed its use.

The method adopted is as follows: On the morning

(6) Report No. 7, Gonorrhea Service, Canadian Hospital, Etchinghill, England.

of the first day a dose of three million of polyvalent gonococcus vaccine is administered subcutaneously and at the same time the seminal vesicles, prostate and Cowper's glands are thoroughly massaged to liberate any toxins confined in them. The patient is then instructed to hold his urine from midnight of that night until a smear is taken the next morning and to do the same for each successive night until four smears have been obtained. On the morning of the second day a dose of five million of the vaccine is administered. Should the case still be infected with the gonococcus, a positive smear may be obtained on one of the four mornings. Should there be no infection with the gonococcus the smear will remain negative for that organism.

TREATMENT WITH ACRIFLAVINE.

Acridine in Treatment of Gonorrhea: an Experimental and Clinical Study. During the course of an investigation by E. G. Davis⁷ and his students of the properties of a large number of compounds with the purpose of finding a drug suitable for use as an internal urinary antiseptic, it was noticed that some of these compounds possessed the property of rapid diffusibility through the tissues. In all, more than two hundred compounds were investigated, many of which were triphenylmethanes, but most of which were synthetic compounds related to sulphthaleins, nearly all of them being highly colored. The rate of renal elimination of each one of these compounds was determined by injection into the ear vein of rabbits, and it was during this procedure that the diffusibility became apparent. Most of the compounds remained confined to the vein into which injected, and passed immediately into the general circulation. An occasional one, however, would spread rapidly from the larger vein into the minute capillaries, and within a very few seconds dye the entire ear a homogeneous color. It was very surprising to observe how the edge of this wave of color would rapidly advance (like a blush) until the ear was completely dyed. Of the entire number of compounds investigated, in about

(7) Jour. Urology, Vol. II., No. 4.

ten this phenomenon was observed. As suggested by Dr. J. T. Geraghty, the ideal drug to be used as an injection in the treatment of urethritis should possess just this property; that is, rapid diffusibility and penetration of the tissues.

Concerning the antiseptic properties of these diffusible drugs many of them are germicidal in high dilution *in water*, but almost all of them lose this property, wholly or partially, when diluted *in urine*. Of the entire number, about a dozen retained their antiseptic action to some extent, and, of these, four were both antiseptic and diffusible, and hence were experimentally indicated as being worthy of trial in the treatment of gonorrhea. These compounds were malachite green, brilliant green, proflavine and acriflavine, of which the last, acriflavine, was found to be antiseptic in the highest dilution of them all. This drug was also among the most diffusible.

Experimentally, acriflavine was shown to possess the much desired property of diffusibility. Moreover, it was found to be antiseptic in urine in higher dilution than any other diffusible dye studied. It inhibits the development of the gonococcus in a dilution of at least 1:300,000 (has at least 600 times the strength of protargol), and therefore a trial of this drug in the treatment of gonorrhea was justified. This part of the work was undertaken by B. E. Harrell.⁸

The ideal drug for the treatment of gonorrhea should cause a minimum of injury to the urethral mucous membrane, should be highly toxic to the gonococcus, and should possess to a high degree the power of penetrating to the deeper structures of the urethra so often involved in this disease. The drugs most often used for this purpose, argyrol and protargol, fulfill these requirements only in part. It was a realization of the shortcomings of our present therapy that these investigations were undertaken.

Urethral injections of acriflavine cause slight smarting which persists for an hour or more. Patients who have had previous treatment with protargol say, however, that it is decidedly less than that caused by the

silver salt. The smarting has never been severe and no patient objected to the treatment. The author used dilutions varying from 1:2,000, to 1:100, but found the 1:1,000 most satisfactory; it is just as efficient as the more concentrated solutions and the smarting is less, in fact with this strength it is almost negligible. There were two cases of retention following the use of a 1 per cent. solution. These patients complained of no pain except that caused by the inability to void. There was evidently no stricture formation as they were catheterized without difficulty and the symptoms promptly disappeared on discontinuing treatment. There was no complication following the use of a 1:1,000 solution.

In the anterior cases the writer injected about 3 c.c. of a 1:1,000 solution into the anterior urethra where the patient retained it for five minutes. In the posterior cases Harrell injected from 15 to 30 c.c. through into the bladder, distending the urethra and having the patient retain the dye in the urethra for five minutes and in the bladder till the next voiding. Injections should be given twice a day until all organisms have disappeared from the discharge and then once a day until the patient is considered well. All the results were controlled by daily examination of smears from the urethral discharge and of the urine voided in three glasses.

Frequently the organisms disappear from the discharge following a single injection and do not return during the subsequent course of the disease. In the majority of cases they have disappeared after two or three injections. In a few cases the organisms disappeared after one or two injections and have been found again later, but have soon disappeared under continued treatment.

The discharge is markedly decreased from the beginning, very quickly becoming thin and mucoid in character. It then gradually becomes less until about the fifth day it has usually disappeared altogether. In a few of the more resistant cases the fragmentation of the leukocytes mentioned by Browning was observed.

	Duration of Disease	Duration of Treatment in Days	Number of Treatments
1	3 days	3	3
2	2 months	3	4
3	4 months	2	2
4	5 months	3	3
5	4 days	5	5
6	6 days	5	5
7	8 months	6	7
8	2 weeks	5	8
9	2 months	5	8
10	?	11	13
11	1 day	7	7
12	2 years	7	7
13	3 weeks	16	16
14	4 months	12	13
15	10 days	14	16
Average.....		6-14/15	7-12/15

In cases of anterior and posterior urethritis it was found that the posterior infection usually improves before the anterior, in fact, it is usual for the urine voided in three glasses to be cloudy in the first and clear in the second and third. The trigonal inflammation also quickly subsides. Cases with frequency and nycturia have frequently had these symptoms entirely relieved by a single injection, nearly always by two or three.

Some of the dye evidently remains in the urethra for a considerable time. The discharge at the end of twenty-four hours is still stained a brilliant yellow and microscopically many of the leukocytes are well stained. The urine is definitely yellow and is fluorescent even at the end of thirty-six hours.

The cases in the table, though some of them gave a history of gonorrhea lasting from a few weeks to two years, have all had a purulent discharge showing intracellular diplococci when first seen. Many of these patients had been receiving treatment since the onset of the disease.

There were recurrences as is the rule with any form of treatment. Treatment was not resumed in these cases till they had developed the maximum of immunity, usually in five to seven days. Treatment at the end of this time has usually given prompt results.

A striking feature of this form of therapy is that in

many cases the dye acts almost as a specific, while in an occasional one it seems without any effect whatever. Such cases are evidently not very common, however, as in the considerable number that were treated there were found only four of this class. Two of these responded at once to injections of protargol. In the third case the discharge was much decreased by acriflavine, but not cured.

Treatment of Gonorrhea with Acriflavine. According to David Watson,⁹ the results obtained in gonorrhea cases were very satisfactory, and this drug now occupies the chief place in the scheme of treatment adopted in the venereal clinics under his control.

The solution recommended for general surgical use (1 in 1,000 in normal saline) was found to be too strong for free application to the urethra. The strength which may be employed for the urethra varies inversely with the quantity of solution used. Thus, when using small quantities by the syringe method of treatment, a concentration of 1 in 1,000 in normal saline may be prescribed, but in lavation ("*grand lavage*" of Janet) 1 in 4,000 in normal saline was found to be the optimum, one pint being used twice daily.

Stock solutions of 1 in 500 acriflavine and of 1 in 6 sodium chloride are kept, and 20 oz. of the dilute solution is prepared for each patient by mixing $2\frac{1}{2}$ oz. of the acriflavine solution, 1 oz. sodium chloride solution, and $16\frac{1}{2}$ oz. warm water (106° F.). The stock solutions are filtered if not perfectly clear.

For anterior urethritis, treatment by syringe injections is simple for the patient to carry out in private practice as compared with lavation by means of a douche can, but it can not be recommended as a routine procedure. The posterior urethra is infected for some time, probably for from one to three days, before definite symptoms of its involvement are manifest, and it is important that treatment of the posterior urethra should not be withheld during this period.

Brilliant results can be attained by 1 to 1,000 acriflavine injections in some cases, but this method neither prevents the occurrence of posterior urethritis nor

(9) Brit. Med. Jour., May 10, 1919.

aborts it, if it exists, and is followed by a larger percentage of complications. During a properly conducted treatment by urethro-vesical lavation, posterior urethritis with its risk of complications does not arise; the onset of prostatitis or epididymitis after lavation has been begun means either that gonococci had previously reached the prostatic or seminal ducts, or some failure in the method of lavage.

The following analysis of the cases of gonorrhea treated in a general hospital during a period when acriflavine was largely employed (January to September, 1918) proves the value of acriflavine lavation.

A total of 423 patients with gonococcus infections were admitted, and the average detention in hospital was 28.8 days. Of these, 307 were cases of acute gonorrhea; of these 116 are classed as chronic, because the disease had been present for one month or more. The acute cases had an average stay in hospital of 26.8 days; in 222 of them acriflavine was the only antiseptic employed; these cases averaged twenty-one days in hospital. Of this group of cases, twenty-six suffered from complications on admission—namely, epididymitis nineteen, rheumatism two, cowperitis two, stricture two, prostatitis one. If these be deducted there remains 196 cases of uncomplicated acute gonorrhea treated by acriflavine lavation. These cases show an average of 19.8 days in hospital; the actual treatment was completed in 15.4 days, and the patients were retained for the other 4.4 days for observation before being dismissed as cured. Of the patients treated with acriflavine, 6 per cent. relapsed; these patients had been, on an average, only eleven days in hospital, and less than seven days under treatment.

When a patient with acute gonorrhea with profuse purulent urethral discharge is put on acriflavine lavation the inflammatory symptoms quickly subside. Within twenty-four hours the discharge has decreased one-third, and by the third day it has usually disappeared, leaving perhaps a trace of moisture expressible in the morning. After three or four days' treatment gonococci are absent from smears taken from the urethra. Nevertheless if the lavage be discontinued at this time discharge and

gonococci will return within a few days in many cases. The treatment should therefore be maintained for from ten to twelve days, when, with the smear negative, no discharge expressible in the morning, and the morning urine showing neither pus nor filaments, all treatment may be suspended. The patient receives a change of underclothing and remains under observation for four days longer, when he may be discharged should no symptoms of relapse have developed.

Adverse Report on Acriflavine in Gonorrhea. Quite another impression of the value of acriflavine in gonorrhea is given by reading the article by John Armstrong.¹ He says that acriflavine is highly diffusible, and that it penetrates the mucosa of the urethra and bladder, that it is an antiseptic of high power, and inhibits the development of the gonococcus in dilutions of 1 in 300,000. There is no doubt that in the laboratory these results can be, and have been, obtained. But few who have had any large experience in the treatment of gonorrhea will agree with the writer regarding its action on the living subject. They state the most satisfactory concentration is found to be 1 in 1,000; that the smarting is almost negligible, and that organisms disappear from the urethra after two or three injections. Armstrong has used this preparation, selecting twenty-three cases of ordinary uncomplicated gonorrhea, carrying out the exact régime laid down by the writers. Of these twenty-three cases, six, or 26 per cent., showed that at the end of three weeks Gram-negative diplococci, morphologically indistinguishable from gonococci, and purulent beads, were present within twenty-four hours after stopping the injection. Of the remaining seventeen, thirteen, or 76 per cent., showed pus cells in their smears, and their anterior washes, which, when centrifugalized, had a purulent deposit. The remaining four showed mucus and epithelium. Far from causing only slight smarting at the strength recorded, the patients treated complained at the end of ten days of severe smarting and dysuria, which has never been a symptom in any cases treated with ordinary solutions of protargol. Armstrong has

(1) Brit. Med. Jour., June 7, 1919.

found that in cases of submucous infiltrations or in soft strictures associated with gonorrhea the remedy is apt to produce retention of urine. The fact of the urine remaining yellow for hours and the leukocytes being well stained is of little clinical significance.

REVIEW OF METHODS OF TREATMENT.

Massage-Pack Method in Acute Gonorrhea. It is now an Australian A. M. C. order that the massage-pack method of early treatment of gonorrhea shall be used to the exclusion of all others.

As the originator of this method, J. P. Fogarty, Major A. A. M. C.,² submits the following detailed account of his efforts and the results obtained.

The object in devising the method was to put into practice a theory that the speediest and the best curative results would be obtained by dressing and draining the infected portion of the urethra, by the application of an antigonococcus chemical to the infected surface, and by preventing the spread of the infection.

To attain these objects, the basis of the treatment consists in packing the anterior portion of the urethra with a material soaked in silver solution. The pack not only absorbs the discharge and drains the infected part, but, by mechanically dilating the urethra, it enhances the prospects of the chemical reaching the site of infection, and prevents apposition between infected and non-infected surfaces.

For packing, soft gauze is far superior to absorbent cotton. It is more absorbent, less irritating, and more easily passed into and withdrawn from the urethra; it has no tendency to break, and shreds are not detached from it.

In the majority of the cases, argyrol has been used, but during periods of shortage silver vitelline has been tried with equally successful if not quite so speedy results.

From a curative point of view, an argyrol solution stronger than 5 per cent. is not necessary, and 7 per cent. and 10 per cent. show a tendency to cause soreness,

(2) Brit. Med. Jour., Nov. 3, 1919.

necessitating less frequent packing, thus depriving the patient of the benefit of the mechanical advantages of the pack. Hemorrhage rarely has occurred, even with 10 per cent. solutions, and not in one single instance with a 5 per cent. solution.

The patient having passed water, and the glans penis and prepuce having been well washed with 1 in 8,000 solution of potassium permanganate, a probe is introduced into the urethra to determine its general direction and whether there is any narrowing or other obstruction.

A strip of soft open woven gauze is cut $\frac{1}{2}$ to $\frac{3}{4}$ of an inch in width and about 7 inches in length. The width of the strip should vary with the size of the meatus, and with experience and practice can be estimated accurately. Having rolled the strip into a cylinder and soaked it in 5 per cent. argyrol, one end is folded over the extremity of a probe and passed up the urethra until resisted at the bend. Thus the whole anterior urethra will be packed. The excess of the pack may be cut off at the meatus.

The procedure is facilitated by opening the meatus with the tips of the thumb and index finger of the hand holding the penis, and by balancing the free end of the strip on the little finger of the hand holding the probe. If the penis be slightly tilted upward and the strip well balanced the loss of argyrol by dripping will be obviated. There is no danger of injury to the urethra if a moderately large probe with a good bulbous extremity be used.

Having packed the anterior portion of the urethra, the penis is then gently massaged for five minutes, all the movements being made toward the root of the penis.

The pack is then withdrawn, the meatus, in so doing, being gently compressed between the finger and thumb in order to leave behind in the urethra as much argyrol as possible.

A second pack is then introduced in the same manner as the first and retained for four hours, or, if the patient does not require to pass water, even longer. While the pack is being retained for four or more hours there is no tendency for the discharge to trickle outwards along its side, and on withdrawal there is no evidence, such

as a flow of pus, to suggest an accumulation of discharge behind the pack. On the other hand, on withdrawal, the pack will have lost most of its argyrol color, and pus, especially in cases with copious discharge, may be easily squeezed from it.

The number of packs given in the day's treatment will be guided by the condition of the case, but as a general rule the pack is indicated with a purulent discharge or with acute subjective symptoms, such as scalding, even before the purulent stage is reached. The majority of the cases have responded to two packs a day (morning and evening), but when necessary, as in a number of cases, three packs in one day are easily tolerable.

The pack is rarely necessary after the fourth morning of treatment. As soon as the discharge, observed before passing water in the morning, ceases or becomes non-purulent (clear watery) the pack should be discontinued and treatment confined to gentle irrigation with 1 in 5,000 potassium permanganate three times a day. The author has applied the treatment to 742 cases of acute gonorrhea.

Apart from the encouraging results—only seven uncomplicated failures in 742 cases (183 out of 184 proved by at least four negative smears in each case)—the method has in addition the following advantages:

1. The ease and simplicity with which it can be carried out.

2. It is comfortable and soothing to the patient, alleviating the sensation of wanting to urinate, and there is much less tendency to painful erections which characterize the condition under irrigation methods.

3. It reduces irrigation and syringing during the acute purulent stage to a minimum, and thus lessens the risk of driving the infection into the posterior urethra or further.

4. It does away with the leakage of the discharge at the meatus and thus obviates the possibility of troublesome balanitis. This condition did not occur once in the series of cases.

5. Withdrawal of a definite pattern on the pack or

the adherence of mucus or shreds will often indicate local areas of disease.

6. It has an economic advantage over other methods, because much less silver solution is required.

A New Principle for Treatment of Gonorrhea. Histologically, in the opinion of F. S. Mason,³ gonococci do not differ from other independent or intradependent cell units, inasmuch as they are made up of a cell wall, cytoplasm, nucleus and nucleoli. It would appear, therefore, that if one can introduce within the cytoplasm some chemical reagent, or "sensitizer" and after sensitization apply a second reagent or "developer" which will bring about within the cytoplasm of the gonococcus cell, a precipitate by intramolecular decomposition, one should be able, probably, by mechanical means so to affect the chromosomes, that mitosis or cell reproduction will be interfered with, if not entirely inhibited. With this thought in mind, Mason sought for a number of sensitizers and developers, which would not be irritating to the urethra, nor affect the surface tension of the cell walls of gonococcus, in fact, which would not be an astringent, or in any way interfere, with the mucosa already infiltrated and inflamed. He first applies with a syringe a sensitizer (which is a solution of chemical substance in physiologic salt solution) which immediately sensitizes the cytoplasm of the cell. One minute is sufficient to sensitize thoroughly the anterior urethra. This liquid is then allowed to run out and the developer used; this also is allowed to remain about one minute within the urethra. This is repeated two or three times daily. After the first or second application, there may be still some pus, but in most cases the gonococci will have disappeared.

The sensitizer and developer which the author has found effective, and has used most extensively is a solution of 1:1,000 toluene diamine in physiologic salt solution as a sensitizer, and physiologic salt solution of 1:1,000 bichromate of potash with 1:1,000 picric acid as a developer.

(3) New York Med. Jour., March 1, 1919.

Mercurochrome—220: A New Genito-Urinary Germicide. Some of the results of the experimental work being carried on at the Brady Urological Institute for the purpose of finding an ideal genito-urinary antiseptic are reported by Young, White and Swartz.⁴ The substance giving the most promising results was found to be "mercurochrome—220," which is obtained by substituting one atom of mercury in the molecule of dibrom-fluorescein. Chemically it is dibrom-oxymercury-fluorescein, or its sodium salt. The latter contains about 26 per cent. of mercury.

The free acid is a red powder insoluble in water but readily soluble in sodium hydroxide solution, with the formation of a deep, cherry-red color, showing fluorescence on dilution. The dry salt forms iridescent green scales, slightly hygroscopic and readily soluble in water. The solution is stable and is not affected by moderate heat or exposure to the air. Strongly acid urine (PH=5.0) gives a slight precipitate *of the free dye*; but if the acidity is PH=6.4 or less, no precipitate occurs. There is entire freedom from precipitation when a 1 per cent. solution of the drug is mixed with an equal volume of medium rich in protein, such as hydrocele fluid. The solution stains the skin a bright red color, but the stain is readily removed by rubbing first with 2 per cent. potassium permanganate solution, and then with 2 per cent. oxalic acid solution.

Mercurochrome—220 is experimentally a drug of great germicidal value. A solution of about 1:1,000 kills *B. coli* and *Staphylococcus aureus* in urine in one minute. It has practically fifty times the germicidal strength of acriflavine in urine medium for exposures of one hour.

In a strength of 1 per cent. the new drug is tolerated by the human bladder for from one to three hours without irritation. Injections of 1 per cent. solution into the renal pelvis are likewise free from pain, even when held *in situ* by plugging the catheter.

That mercurochrome—220 has a remarkable germicidal value is shown, the authors state, by the rapid steriliza-

(4) Jour. Amer. Med. Ass'n., Nov. 15, 1919.

tion accomplished in a series of cases of cystitis and pyelitis of long standing and refractory to other treatments. Now for the first time we have a method of quickly curing certain chronic infections of the bladder. The rapidity with which a few cases of old purulent cystitis disappeared was surprising.

Studies of the comparative value of acriflavine and mercurochrome—220 in gonorrhea are not yet complete, but it has been demonstrated that with both drugs, methods of great value in the treatment of the disease have been produced.

Mercurochrome—220 has proved, the authors say, to be eminently satisfactory in the treatment of chancroids and as a dressing for buboes after incision.

Normal Horse Serum in Acute Gonorrheal Epididymitis. In the *Naval Medical Journal* of January, 1918, an account was given of observations made by R. A. Brown on the therapeutic value of antidiphtheria serum in the treatment of gonorrheal epididymitis. It was pointed out that antidiphtheria serum had been employed, because as an empirical expedient, it had been found effective in the treatment of other conditions, which had no recognizable relationship with diphtheria infection. It then occurred to Brown⁵ that normal horse serum might have an equally beneficial influence.

At the time of the completion of the observations referred to in that paper a new series of observations had been commenced in which normal horse serum was being employed, and during the past year these observations have been carried out in 100 cases.

In order to constitute a basis for comparison with the previous results, an amount of horse serum equal to the amount of antidiphtheria serum previously employed was injected at corresponding intervals; that is to say, instead of injecting 5 c.c. of antidiphtheria serum, an injection of 5 c.c. of normal horse serum was given every twenty-four hours for five days. It was found that the employment of normal horse serum in this amount had no recognizable therapeutic influence.

(5) Glasgow Med. Jour., November, 1918.

The dose was then increased to 10 c.c., administered every twenty-four hours for five days, and here again the therapeutic results had practically no value.

It was not until the amount administered reached from 40 to 50 c.c. daily for five days that good results were obtained.

The results which have emerged from the observation of 100 selected cases comparable with those observed in the first paper are that 200 to 250 c.c. of normal horse serum are required to produce the therapeutic effects obtained by 25 to 30 c.c. of antidiphtheria serum.

Taking the results as a whole, normal horse serum in the amounts indicated gave results as good as the antidiphtheria serum; and there was only one case in the 100 in which the amelioration of the symptoms was not progressive during the week through which the treatment was carried out. In this case an improvement occurred for the first three days, and on the fourth day there was a relapse. The treatment, however, was continued, and at the end of the week the symptoms had disappeared.

An important observation in the comparison of the two series was that while antidiphtheria serum in the small amount produced an obvious constitutional reaction, indicated by fever and sweating, there was no such constitutional reaction following the use of the large amount of normal horse serum; at least in so far as the appearance of symptoms was concerned, although erythema appeared in some cases during treatment, and probably in many others after they were discharged south when the symptoms of epididymitis had gone.

Gonorrheal Complement-Fixation Test. The Gradwohl modification⁶ of the Hecht-Weinberg complement-fixation test for syphilis has been found by Gradwohl⁷ to be equally valuable in the complement-fixation test for gonorrhea. The only change necessary in the test is the substitution of the gonococcus vaccine for the syphilitic vaccine.

(6) Practical Medicine Series, 1917, Vol. IX., p. 188.

(7) New York Med. Jour., Nov. 30, 1918.

Altogether 158 samples of blood were examined by both the new and old techniques. A number of these blood specimens were introduced into the study as controls. In most instances no details of the history of any of the cases were known before the results were reported. Many of them were candidates for matrimony, giving every evidence of a clinical cure. There were a number of cases of women recovering from curettement after abortions, with no history or symptoms of gonorrheal infection. There were seventy-nine male blood specimens and seventy-nine female. In seventy-seven cases a negative reaction was obtained by both methods. In sixteen cases, he obtained a strong positive reaction with both methods. In sixty-nine cases he obtained a clear negative reaction with the older method, and a strong positive with the new method. In three cases, an insufficient amount of blood was submitted to make both tests, therefore these three cases are eliminated from the figures. In other words, the older technique yielded but 20 per cent. of positive reaction in patients unquestionably harboring gonococci, whereas the technique described yielded 100 per cent. of positive reactions in these sixty-five cases. This means that the new method is 80 per cent. more accurate than the other method. Gradwohl does not wish to be understood, however, as stating that the new method yielded 100 per cent. positive in all gonorrheal cases in which a reaction was to be expected.

CHANCRIFORM LESIONS.

EXTRAGENITAL CHANCROIDS.

Triple Chancroids of the Hand. Last year we noted in this volume the occurrence of a professional inoculation chaneroid on the hand of a physician.¹⁰ The same author, Milian,¹ describes the case of a young officer who was admitted to the hospital with a lesion about the nail of the left index finger which was supposed to have been an ordinary pus infection and was so treated

(10) Practical Medicine Series, 1918, Vol. VII., p. 165.

(1) Ann. des mal. vén., December, 1918.

by the surgeon for some time. When the patient was transferred to the service of Milian, he immediately thought of chancroid and demonstrated the bacillus of Ducrey. Seven days after the appearance of the lesion on the tip of the finger another appeared at the base of the same finger. Nine days later, following a deep abscess, another lesion developed on the back of the hand.

The clinical appearance of the chancroids was typical. The most marked symptom was the pain which was so intense that the patient was unable to sleep without sedatives. All the lymph glands of the left arm, axilla, and cervical region were markedly enlarged and indurated, but no bubo developed. Even the left tonsil took part in the enlargement.

The patient had had intercourse at repeated intervals with the same woman for some time. Owing to the fact that no infection of the penis took place it was assumed that the vulva was free from infection, and that the infection on the finger resulted from insertion of his finger into the anus of the woman.

Chancroid of the Finger. The report of extragenital chancroids by Milian is followed by another case report made by L. B. Gerbay.² In the course of the treatment of 15,000 venereal cases in a venereal center the author has seen but one chancroid lesion of the finger, notwithstanding the fact that there were 2,000 cases of genital chancroids. From these figures it is evident that chancroid of the finger is an extremely rare occurrence. The case observed by the author occurred in a man 22 years old who had a soft chancre of the penis which he was required to dress each day. It is supposed that during the course of the dressing he managed to infect his finger. There was intense pain, which interfered with sleep. Potassium permanganate solutions, together with silver nitrate and iodoform led to healing.

CHANCROIDS SIMULATING CHANCRES.

Chancroids Simulating Chancres. The complications which may arise in diagnosis as a result of cauterization

(2) Ann. des mal. vén., May, 1919.

of a simple ulceration of the penis are illustrated by a case observed by Thielmanns.³ The patient was a Belgian soldier 30 years old who had had gonorrhea for two years prior to coming under observation and had suffered from herpes progenitalis at frequent intervals. During one of these attacks he had intercourse, after which he cauterized the herpetic lesion with alum. When examined about twelve days after coitus there was a small, indurated lesion on the glans. On the balano-preputial border there was an ulcer which had a macular, infiltrated base of cartilaginous hardness, and which was very tender and painful, and was bathed in pus. In the right inguinal region was a group of enlarged glands. Inasmuch as the medical officer was in a combat unit there was no opportunity for making a dark-field examination. The soldier was kept under daily observation, however, and the progress of the ulcer carefully watched. No secondary rash appeared and after about four weeks the ulcer healed and the induration was absorbed.

CHANCERIFORM LESIONS DUE TO GONOCOCCUS.

Chancriform Lesions Due to the Gonococcus. Ulcerations strongly simulating the primary lesion of syphilis due to the gonococcus were probably first described by Jullien at the Congress of London in 1896. Burnier⁴ reviews the literature on this subject and reports the observation of several such cases. These lesions occur in both men and women and in patients who have had gonococcus urethritis before the appearance of the ulceration. As a rule the ulcerations occur on the glans penis near the meatus. They are usually oval or circular erosions of irregular outline, of deep red color, and superficial ulceration. As a rule they suggest the soft chancre, but they may have a deep, indurated base, simulating the hard chancre. Associated with the lesion is inguinal adenopathy, either unilateral or bilateral, with or without suppuration. The diagnosis of these lesions is fa-

(3) *Ann. des mal. vén.*, October, 1918.

(4) *Ibid*, February, 1919.

cilitated by the existence of the urethritis prior to the onset of the ulcerations, and microscopically by the demonstration of the gonococcus. The treatment consists essentially of applications of strong permanganate of potash solutions, or of silver nitrate.

Chancriform Vaccine Erosions of the Vulva. The development of umbilicated vaccinal pustules far removed from the point of inoculation is not uncommon. The most frequently involved areas are the face, the lips, the extremities and the abdomen. In general these lesions are the result of accidental inoculation. An unusual localization was observed by E. Ozemar⁵ of Toulouse. The patient was a woman 24 years of age who, fearing the effects of vaccination, urinated on a handkerchief at frequent intervals and attempted to prevent the inoculation by swabbing off the scarified area on the arm. Nine days after the vaccination the arm became swollen and painful and an umbilicated pustule appeared. On the following day a number of umbilicated pustules appeared in the vulva accompanied by a sharp rise in temperature, headache and vomiting. The marked swelling on the left side led to a provisional diagnosis of a chancre, which was later corrected by a more careful examination.

Antimony Tartrate in Chronic Secondary Chancroid Ulceration. In tropical countries, extensive secondary ulceration in the inguinal regions, following primary infection by the bacillus of Ducrey, is not very uncommon. Some cases, so severe in character as to necessitate them being invalided home, occurred amongst Australian soldiers on active service in Egypt. These cases had proved quite unresponsive to the various forms of treatment adopted, and during many months almost every conceivable form had been tried. Intravenous injections of potassium-antimony-tartrate as recommended by J. R. McDonagh, were then administered by W. L. Potter,⁶ and resulted in rapid and complete healing.

(5) *Ann. de dermat. et de syph.*, December, 1919.

(6) *Med. Jour. Australia*, July 27, 1918.

SYPHILIS.

THE CHANCRE.

An Analysis of Fifteen Hundred Chancres. An interesting study of 1,500 cases of syphilitic chancres had been made by Levy-Bing and Gerbay,⁷ who were in charge of one of the venereal centers of the French Army. A careful examination of the patients showed that of the 1,500 cases only 386 infections had occurred in the war zone, whereas the remaining 1,807 occurred in the zone of the interior. There were twenty-seven cases in which it was absolutely impossible to determine the origin of the infection. In these cases, 1,227 chancres occurred as the result of contact with women of the streets; 161 chancres were contracted from women in public houses; eighty-one were of conjugal origin, and thirty-one cases gave such an indefinite history that it was impossible to determine which of several women might have been the source. The youngest patient was nineteen and the oldest forty-eight years of age. Of the 1,500 cases, only ninety-two were evacuated to the interior, and these evacuations occurred because of intercurrent infections. The average duration of the hospitalization was thirty-six days; in general from eight to fifteen days had elapsed before the date of hospitalization. Unfortunately, in many cases this delay had been still greater, but a few cases were seen within two days of the appearance of the chancre. One case had existed only twenty-four hours and began as a lesion which closely simulated the vesicle of herpes progenitalis.

An interesting phase of the study of this group of chancres was an attempt to apply the law of probabilities, which was first evolved by Gauss, to a determination of the probable date of contamination. By taking a group of cases in which they were able to determine definitely the incubation period, they constructed a chart on which the curve coincided with that of the law of Gauss. This is probably one of the first attempts to apply the law of probabilities to a biologic problem. It

(7) *Ann. des. mal. vén.*, June, 1919.

is understood, of course, that the tables which they have worked out prove nothing, but they are interesting for purposes of speculation when the patient has been exposed on several different occasions all of which fall within the time limit of the incubation period. The following table will be found convenient in determining which one of several exposures is probably the contaminating one:

TABLE OF INCUBATION PERIOD PERCENTAGES.

x	P	x	P	x	P	x	P
10	1	23	13	36	58	49	94
11	1	24	16	37	62	50	95
12	1	25	18	38	66	51	96
13	2	26	21	39	69	52	97
14	2	27	24	40	73	53	97
15	3	28	27	41	76	54	98
16	3	29	31	42	79	55	98
17	4	30	43	43	82	56	99
18	5	31	33	44	84	57	99
19	7	32	42	45	87	58	99
20	8	33	46	46	89	59	99
21	10	34	50	47	91	60	100
22	11	35	54	48	92		

In this table under "x" is given the number of days and under "P" the percentage of cases which ordinarily will be found having this period of incubation. For example, opposite "x" 38 we see under "P" 66. That means that about 66 per cent. of the cases of chancres develop by the thirty-eighth day. By consulting this table one is able to fix the limits within which the incubation period of a given chancre will probably fall. By a process of calculation it can be shown that the percentage of cases having a given incubation period will be as follows:

From 10 to 15 days.....	2 per cent.
" 15 " 20 "	5 " "
" 20 " 25 "	10 " "
" 25 " 30 "	16 " "
" 30 " 35 "	20 " "
" 35 " 40 "	19 " "
" 40 " 45 "	14 " "
" 45 " 50 "	8 " "
" 50 " 55 "	3 " "
" 55 " 60 "	2 " "

There remain 1 per cent. of cases having an incubation period of less than ten days or more than sixty days. As a practical application of this method of calculation the following case is cited: A syphilitic has a chancre developing on the first of June. Preceding the development of the chancre he had two exposures, both of which appeared to him equally infectious. The first exposure occurred some time between the fourth and fifteenth of April, the second exposure some time between the third and twelfth of May. The solution of the problem would be something as follows: If the contamination occurred at the time of the first exposure the period of incubation would fall between forty-six and fifty-seven days. If it occurred on the second exposure the duration of incubation would fall between nineteen and twenty-eight days. Consulting the first table we find under "x" the number 46 to 57. Opposite to these numbers we find under "P" the numbers 89 to 99, the difference of which is 10. Dividing this difference by the difference between the number of days

$$(57 - 46 = 11) \text{ we find } \frac{10}{11} = 0.91.$$

By a repetition of the same calculation for the second exposure we look opposite 19 and 28 and find the numbers 7 and 27, of which the difference is 20, and we have here

$$(28 - 19 = 9) \frac{20}{9} = 2.22.$$

The latter number is larger than the first; from this it may be concluded that the second exposure is more probably the contaminating one. There are, in other words, twenty-two chances against nine that it is the origin of the chancre. It is understood, of course, that one could not be sure that the second exposure had given rise to the chancre; even if the chances were a thousand to one that such was the case it would be nothing more than a probability. There would be no proof that such was the case.

Among the 1,500 chancres the lesion was unique in 1,141 cases. There were 359 cases having one or more chancres. The maximum number of multiple chancres was ten. In exactly 23.9 per cent. of the cases there were at least two chancres. The high percentage of

multiple chancres in these soldiers was supposedly due to the insufficient opportunities for cleanliness, and the wide prevalence of scabies and traumatic dermatoses. Amongst the 359 cases of multiple chancre practically all the chancres developed simultaneously. The period of time elapsing between the appearance of the multiple chancres was as a rule not more than three days. Only in one case had five days intervened between the development of two chancres.

Extragenital chancres were extremely rare. In a total of 2,185 chancres there were about fifty-eight extragenital lesions. The tabulation of these extragenital chancres follows:

Lips	
(superior	13
(inferior	10
(commisures	2
Gums	2
Tonsils	2
Tongue	5
Chin	1
Nose	1
Ear	1
Cheek	1
Arm	
(hand	2
(fingers	5
Leg	1
Abdomen	10
Perineal region	2
	<hr/>
	58

The chancres encountered, as a rule, presented the classical picture of a circular, erosive, indurated lesion, but in some cases one or more of these essential characteristics was lacking. The authors insist on the fact that no classical sign is constant, and frequently all of the laboratory researches must be called upon before a diagnosis can be established. The size of the chancres varied between wide limits. It may be the size of a pin-head, or it may measure 6 cm. in diameter. The induration is almost always present and constitutes a symptom of undoubted value. In some cases, however, it may be atypical, nodular, or without sharp demarcation, and in

some cases the induration may be entirely lacking. The same is true of the regional adenopathy, which may be very slight or very pronounced.

[The importance of determining the probable source of contamination is self-evident in these days when so much is being done toward eliminating sources of infection. A number of states have state laws which enable the Department of Health to hospitalize persons who are infectious. Therefore, if it can be determined which one of two women or of two men is at fault it would be of value in bringing about the treatment of that individual.

The importance of an early search for spirochetes by the dark-field method can not be too often emphasized. We have passed the day when we wait for the secondary manifestations to appear, or for the Bordet-Wassermann to become positive. There are even now all too many men who, when first the chancre comes under their observation will refer the patient to a laboratory for a blood test rather than for the dark field examination. As a rule, the earlier treatment is begun the better the prognosis, and therefore every genital ulceration should be examined immediately for spirochetes, even if it has the appearance of being nothing more than an herpetic eruption.—M.]

Two Urethral Chancres Mistaken for Urethritis. Urethral chancre is extremely rare, as shown by the figures of Levy-Bing and Gerbay, who found but one urethral chancre in a series of 2,127 chancres of the genital region. Montpellier^s saw two cases, both of which were diagnosed at first as gonorrhea. Both patients had had previous attacks of gonorrhea and both developed slight discharge after the exposure. An interesting feature of the two cases was the very short period of incubation. About the fifth day after exposure there was a marked oozing and by the twentieth day there was a sufficient amount of induration to be palpable. One of the patients occurred after *coitus ab ore*.

Coexisting Chancres of the Gum and Clitoris. Chancre of the gum is rare as shown by the series of Four-

(8) Ann. des mal. vén., June, 1919.

nier, in which there were but eleven cases in a series of 729 buccal chancres. In the series of Goucher there were two out of a total of 87 cases. Duncan Bulkley found forty-two in a group of 1,810 initial lesions of the mouth.

Montpellier and Lebon⁹ report a case of chancre of the gum about the left upper canine tooth which developed about the same time as a chancre of the clitoris. As a rule every patient with a chancre about the mouth or lips will attempt to incriminate a dentist or to explain the inoculation on the basis of the use of a toilet article belonging to another person. In this case, however, the patient, who was a woman 42 years of age, frankly admitted *coitus ab ore*.

Multiple Chancres of the Penis. Going through the literature of the past ten years, J. C. Sargent¹ was able to find only one case report of multiple chancres, that of Zeisler. Sargent's case is interesting inasmuch as the two chancres did not develop simultaneously, but four weeks apart. The second chancre, therefore, was either the result of an auto-inoculation or of another exposure.

[In this volume for 1918, p. 178, is an abstract of an article by Bodin in which he reports the finding of 111 cases of multiple chancres in a series of 627 cases of primary lesions. The lesions did not all develop simultaneously in a given case.—M.]

EXTRAGENITAL CHANCER.

Extragenital Chancre Arising in Line of Duty. Two interesting cases of accidental inoculation arising in the line of duty are described by Gougerot, Lévy and Clara.² In one case the chancre developed on the left side of the upper lip of a telephone operator at the point where the receiver came in contact with the mouth when the combination receiver and transmitter was held in the left hand. In the other case the chancre developed on the upper gum. This patient was a cook who made a

(9) Ann. des mal. vén., April, 1919.

(1) Jour. Amer. Med. Ass'n., Jan. 11, 1919.

(2) Ann. des mal. vén., March, 1919.

practice of blowing through a bayonet scabbard for the purpose of starting the fire. It was assumed that another cook had used the scabbard and had deposited thereon spirochetes from his mucous patches.

Chancres of the Fingers and of the Palm. Last year Levy-Bing and his co-workers reported two cases of chancre of the finger, one of which was venereal and one accidental. This year the same authors³ report the observation of more chancres of the hand. In the first case there were two chancres on the index finger, one of which was on the dorsal surface and the other on the palmar surface of the same finger. The infection had occurred from a bite by another soldier.

In the second case there existed a chancre of the index finger of the right hand, another of the palm of the right hand and a third one on the penis, all developing simultaneously and following one exposure. The occurrence of a chancre on the palm is extremely rare.

In the third case the chancre occurred on the dorsal surface of the index finger in some manner undetermined.

Anal Chancre Resulting from Pederasty. An anal chancre resulting from pederasty in a boy 17 years old is reported by C. H. Marshall⁴ of the Department of Dermatology, University of Michigan. Five weeks after the exposure he noticed pain and slight hemorrhage on defecation, which increased in severity until it became almost unbearable. Six weeks later an eruption appeared over the entire body. He developed severe nocturnal headaches and abdominal pain. Dark-field examination of the anal lesion revealed a large number of *Spirochaetae pallida* and a Bordet-Wassermann reaction on the blood was strongly positive. A psychiatric examination was made for the purpose of determining any homosexual tendency in the patient, but was negative.

Prognosis of Extragenital Chancres. Benario found a predisposition for cephalic chancres to *neurorécidive* after incomplete arsenical treatment. In 202 cases of recurrence he found that fourteen, or 7 per cent., occurred in cases of cephalic chancres. Fournier, how-

(3) Ann. des mal. vén., February, 1919.

(4) Amer. Jour. Syph., July, 1919.

ever, says in his work "*Les Chancres Extra-Génitaux*" that the prognosis for extragenital chancres is exactly the same as for genital chancres. Dujardin⁵ made a careful study of the spinal fluid in a series of fifty-three cases of extragenital chancres, most of which were cephalic. He attempted to study three phases of this subject: First, is the secondary meningeal reaction more severe in cephalic chancres than in genital chancres? Second, in cases of insufficient arsenical medication are the neurorecurrences more to be feared? Third, do extragenital chancres offer more resistance to treatment?

He concludes from the study of the first question that in certain cases changes in the spinal fluid may take place earlier in cephalic chancres than in genital chancres, but the spinal fluid changes are practically the same for all cases. Study of the second question leads him to conclude that there is no predilection for cephalic chancres to cause central nervous system involvement. There was no evidence which the author could find which would lead him to conclude that an extragenital chancre offered a more unfavorable prognosis than the genital. In his opinion, the study which he made of fifty-three cases confirms the statement of Fournier.

Early Diagnosis of Syphilis. An analysis of 115 cases of primary syphilis seen at Camp Upton has been made by Major Klauder.⁶ The average duration of the chancres in this series was 34.4 days. The secondary eruption was present in 24.7 per cent. of the cases. Prior to coming under observation, local treatment had been applied in 66 per cent. of the cases. Of the three means at the disposal of the clinician for the early diagnosis of syphilis—namely, the demonstration of the organism, the Bordet-Wassermann reaction, and the clinical appearance—the first is by far the most valuable. A positive dark-field examination was obtained in 57.1 per cent. of the series. The shorter the time elapsing between the onset of the chancre and the examination, the higher the percentage of positive results. In 25 per cent. of the cases the author was unable to make a search for spirochetes because the initial lesion was situated be-

(5) Ann. de dermat. et de syph., July, 1919.

(6) Jour. Amer. Med. Ass'n., March 8, 1919.

neath an inflamed or adherent foreskin, or *the chancre was entirely healed.*

The too common practice of treating genital chancres with a spirocheticidal drug before they are properly diagnosed may prevent or greatly delay the demonstration of the organism. A routine dark-field examination of every genital lesion as a means to an early diagnosis should be a hard and fast rule.

A positive Bordet-Wassermann reaction was obtained in 74.1 per cent. of cases in this series. Both laboratory tests were negative in 8.6 per cent. Therefore, by the use of both tests 91.4 per cent. of the cases of early syphilis were diagnosed by laboratory methods alone. However, by the use of these tests alone, delay may be experienced before the spirochetes are found in the secretion from the chancre, or before the Bordet-Wassermann reaction, if negative, becomes positive. Treatment is therefore delayed, and delay at this critical time may be fatal to a successful outcome of the management of the case. In the absence of positive results with both tests, and the clinical appearance of the lesion is that of a chancre, treatment should be instituted at once, thereby giving the patient the benefit of the doubt.

[The author says that spirochetes can not be demonstrated in the chancres which are concealed beneath an inflamed foreskin, or in those the surface of which has healed over. Repeatedly in the editorial comment in these volumes attention has been called to the technique which is designed for just such cases. A very fine needle fitting snugly to a good Luer syringe should be sent into the lesion at the point, if the chancre be concealed, where the induration is felt to be the greatest; or, if the chancre be on the surface, at the base of the lesion. If a large needle is used so much blood will be aspirated that the finding of the organisms will be rendered impossible. Gentle aspiration for a period of from five to ten minutes, meanwhile turning the needle from place to place, and constantly guarding against drawing of blood, will result in the collection of a good-sized drop of clear serum in the syringe which will be found to be free from the debris and pus organisms so common in the serum which has been collected from the

surface of the genital chancre, even when well cleaned. With this method, the spirochete can be found in 100 per cent. of chancres which have not been treated with arsphenamine. Application of spirocheticides to the surface will not destroy the organisms at the base of the induration, and they can be aspirated with slight, if any difficulty.—M.]

Acquired Syphilis in Moroccan Children. Acquired syphilis in Europe and in America is essentially a disease of adults, and in about 90 per cent. of the cases is of venereal origin. When brought into the family by a careless or indifferent parent the children may acquire the disease, but this is relatively rare. Decrop and Salle,⁷ in an interesting article, show the remarkable frequency of acquired syphilis in the children of Morocco. In the opinion of the writers, syphilis is probably to be found in 75 per cent. of the natives of the cities, most of whom have received little or no treatment, because of the inherent fatalistic view of the Arab.

One might think *a priori* that the frequency of syphilis in the parents might lead to immunity of the offspring and to a gradual disappearance of the disease among the natives. The authors' experience, however, shows that this is not the case. Reinfections are repeated from one generation to another and most of the syphilitic infants seem to have acquired, rather than to have inherited the disease. Chancres are very frequently observed in children. Of 165 cases of infantile syphilis there were seventeen primary lesions, as follows:

Genital organs	6
Lips	3
Tongue	2
Tonsils	5
Legs	1

There were sixty-one secondary cutaneous lesions; one hundred and twenty-two secondary mucous lesions and six other secondary manifestations.

Because of the precocity of puberty in the Arab, the authors concerned themselves only with patients from

(7) Ann. des mal. vén., July, 1919.

one to twelve years of age (first and second infancy). Above this age there were observed 387 cases, divided as follows:

A. Primary lesions	58
B. Secondary cutaneous lesions.....	174
C. Secondary mucous lesions.....	174

The frequency of the mucous manifestations in the figures is striking. The mucous lesions will exist for a long time in the labial commissures and on the margins of the tongue with a minimum of subjective signs. Because of this it is obvious why so many familial infections occur. As an example of the great number of familial cases which occur, they cite the case of a patient 1½ years old who was brought in with a chancre of the upper lip. Examination of the family disclosed the fact that two other children, one aged 4 and the other aged 2, had mucous patches with primary lesions of the tonsils.

A suckling infant 4 months of age in another family had mucous patches in the labial commissures and a papillomatous lesion on the tip of the tongue. The mother was found to have a chancre of the right nipple.

Another patient 2 years old had mucous patches of the labial commissures and of the tongue. A sister 7 years old had a chancre of the tonsil and a papular eruption on the body. A slave of the household, 17 years old, also had a secondary eruption.

A remarkable feature of the familial infections is the similarity of the type of eruption. A patient 2 years old was seen with a hypertrophic papular disseminated eruption with adherent, dry crusts on the back of the arms and about the mouth. A sister 8 years old had similar lesions in the folds of the elbow and on the neck. The mother had a very large similar lesion on the back of the left hand.

The opportunities for contagion among the Arabs are innumerable. The gargoulette is a carafe of porous earthenware in which the water is kept cool. This is covered with a piece of cloth to which everyone applies his lips in drinking. The spoon is passed from mouth

to mouth about the platter. The copper cup containing water is placed so the passer-by may have a drink. The barber-surgeon practices his circumcisions (three primary lesions were the result of this practice) and also carries from head to head the favus fungus. Moreover, the innumerable excoriations due to pediculosis, scabies, and impetigo, among the infants offer excellent portals of entry for the spirochete.

The primary lesion in children is almost always extragenital, except in those cases arising from circumcision. After circumcision the chancre develops in the ring following the cicatrix of the operation. The most frequent portals of entry are the lips, tonsils and tongue.

Syphilis Infection Two Years After the First Infection. Many physicians have expressed doubts as to the curability of syphilis. It is important for the profession to have placed before it as much convincing evidence pointing to the radical extermination of syphilitic infection as possible, in order that there may be developed a crystallized scientific judgment on this important question. There is every reason to believe that many patients treated intensively in the early primary stage are cured, for they commonly remain free of symptoms for years and repeatedly have negative blood tests.

A case of reinfection which seems to be well established is reported by Schamberg.⁸ The patient came under his care Sept. 9, 1917. Three days later the Wassermann reaction with cholesterol antigen was ++++ with alcoholic extract of syphilitic liver, +, and with acetone insoluble lipoids ++++. Between Sept. 22 and Nov. 15, 1917, the patient received eight intravenous injections of the arsenobenzol brand of arsphenamin. The Bordet-Wassermann reaction became negative after the first injection, but relapsed to a weak positive on several subsequent occasions. The patient was drafted into the army, and while at two southern camps, because of a deep scar on the glans penis, had a blood test taken monthly for nine months. All of these tests proved negative. After his discharge from the army, he again lived with a woman with whom he had been

(8) Jour. Amer. Med. Ass'n., Sept. 13, 1919.

living before he entered the army. April 4, 1919, he appeared at the Schamberg clinic at the Polyclinic Hospital with a generalized, pinkish-red roseola. This developed within a fortnight into an extensive varioliform syphilide, covering the face, trunk and extremities. There was a large chancre on the foreskin opposite the corona, a site different from that of the first chancre. Six Wassermann tests made between April 26 and May 26 were strongly positive (+++++) despite seven administrations of arsphenamine and neo-arsphenamine. During this period, the chancre and eruption promptly disappeared under the treatment (Plate XX).

This case is all the more remarkable in view of the fact that during the first attack the patient was irregular in his attendance at the University Hospital, and that, through neglect, he developed what were, in all likelihood, evidences of an early meningeal involvement, characterized by headaches, inequality of the pupils, and exaggerated patellar reflexes. It is interesting to observe that not a vestige of immunity against the second attack remained. Indeed, the second attack was more severe than the first, and the Bordet-Wassermann reaction bids fair to be more resistant to treatment than during the first attack. In this case, the evidence of a second attack seems indisputable. The deduction that the patient was cured of his first attack appears warranted by all of the facts.

Cases of this character are most instructive in the light they throw on the curability of syphilis. The excellent pathologic researches of Warthin at Ann Arbor were persuading many physicians to believe in the dictum enunciated many years ago (under a different therapeutic regimen), "Once a syphilitic, always a syphilitic." Now we are in a position at the present day, with more powerful and scientific drugs at our command, to state that syphilis is a curable disease. The criteria of cure are difficult to establish, because the evidential value of negative Wassermann tests is not conclusive. In view, however, of cures such as the one above reported, we may perhaps place more faith in repeatedly negative serologic tests and the absence of symptoms as indications of probable cure.

Syphilitic Superinfection. Since the advent of ar-sphenamin the possibility of syphilitic reinfection has been much discussed and a great many cases have been suspected or proved to be cases of reinfection. Pinard⁹ saw a young man in October, 1918, who came to his clinic for scabies and was found incidentally to be suffering from a primary lesion with secondary manifestations. He was given a series of six intravenous injections of arsphenamin. The infection had been contracted from his wife while on furlough. He continued to see his wife at infrequent intervals and in June 1919 there appeared a small ulceration on the penis. The lesion gradually enlarged in size and crusted over. Subsequently there appeared squamous and crusted lesions upon the trunk, which suggested a secondary eruption. The Bordet-Wassermann at this time was found to be positive, but unfortunately there was no test made after the first series of injections and before the second lesion appeared on the penis. The author is of the opinion that it was not a reinfection but a superinfection which closely simulated a reinfection. Apparently the superinfection was contracted from his wife who had been receiving little or no treatment.

A Rare Case of Syphilitic Contagion. A case of syphilis which is interesting because of the age of the woman from whom the man contracted the disease, is reported by Malherbe.¹ A very small woman who gave her age as 70 years and who looked even older, presented herself to the author with a request for an examination. She said that her paramour had contracted syphilis through his relations with her and she wanted a thorough examination and treatment if necessary in order that no further damage might be done. A thorough physical examination was carried out, with negative findings for syphilis. There was marked atresia of the vulva and the usual senile cutaneous changes. The patient stated that her paramour was a man 65 years old, whom she had known for forty-five years, and with whom she had had intercourse at regular intervals for the past thirty years. She also stated that at the age of 20 she had

(9) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(1) Ann. des mal. vén., September, 1919.

contracted syphilis and had received very little treatment for the infection.

At the request of Malherbe the man presented himself for examination and was found to have florid secondary syphilis. He stated that he was subject to herpes pro-genitalis, that he had no relations with any other woman in the past thirty years, and that recently he had had a great deal of irritation due to the herpes, and because of the atresia the woman had had several hemorrhages recently after intercourse. The author satisfied himself that both the man and the woman were stating the facts, and that it was a case of syphilis contracted from a woman who had had the disease for approximately fifty years, and in whom the infection had been so mild that practically no pathologic changes had occurred.

[It is ordinarily believed that a patient with syphilis ceases to be a source of contamination after two or three years, even in the absence of treatment. This, however, we now know to be erroneous. Patients may develop mucous patches even during treatment and there are cases reported in which infection has occurred after thirty years. Spirochetes have been found in the seminal fluid of men who have had the disease for a great many years, and no doubt many women are infected from such a source.—M.]

SECONDARY MANIFESTATIONS.

Purpuric Roseola. A chancre of the lip followed by a petechial roseola is described by Levy-Franckel.² The chancre on the lip was an enormous lesion which occupied practically the entire lower lip and had been present for a month. On the body were two types of lesions; a papular syphiloderm and the purpuric lesions. The former were especially numerous on the face, whereas the latter were more numerous on the chest and thorax. The mucous membranes were free from hemorrhage, there was no epistaxis and no evidence of hemophilia. The coagulation time of the blood was not retarded. The patient was not suffering from malaria

(2) *Ann. des mal. vén.*, July, 1919.

and had taken neither mercury nor potassium iodide before coming under observation. The author is able to eliminate the rheumatoid purpura from this case because of the absence of arthritis and because the purpuric lesions promptly disappeared with intravenous medication.

Fulminating Syphilis. An unusually virulent syphilitic infection was observed by J. B. Gooken.³ The patient was a white male 24 years of age, who presented skin lesions, gumma of bone, gumma of lung, and hepatic-visceral involvement, simultaneously and within nine weeks of the appearance of the initial lesion and with the chancre still apparent. Along with this general and acute infection the hirsute areas were spared, as was also the nervous system.

It is also noted that the infection which so vigorously attacked its new host was acquired from his wife, who herself offered no visible signs of the disease. Also, that whether or not increased virulence or lack of resistance was responsible for the fulmination of the infection, it responded to antiseptic treatment quite as readily as the milder manifestations of syphilis.

LATE MANIFESTATIONS.

Diffuse Syphilitic Mastitis. Diffuse syphilitic mastitis is relatively rare compared with gumma of the mammary gland. Such a case is reported by Burnier.⁴ The patient was a woman 42 years old who had never been pregnant and as far as she knew had suffered no traumatism. The onset was slow and the patient first noticed that the gland was becoming hard and firm, although there was no sensation of any kind. The first physician she consulted advised radical operation because he thought it was a maglignant neoplasm. Coming under the observation of the author, syphilis was immediately thought of and the Bordet-Wassermann test was found to be positive. The patient was given a series of mercurial injections without much improvement. Later in-

(3) Amer. Jour. Syph., January, 1919.

(4) Bull. Soc. franc de dermat. et de syph., 1919, Nos. 5 and 6.

travenous injections of arsphenamin resulted in prompt healing.

Orientation of Syphilitic Lesions by Alcohol. It is a common belief that Algerians do not suffer from central nervous system syphilis. Last year, however, a series of spinal fluid examinations was made by Montpellier⁵ who showed that changes take place in the spinal fluid in about the same proportion of syphilitics in Algiers as in Europe. Lacapère⁶ tabulates 2,850 native patients. In all of these, only fifty-seven cases of visceral syphilis occurred. The European has, as a rule, very mild cutaneous involvement whereas the visceral and central nervous system involvement is very grave. In the Arab, on the contrary, cutaneous and osseous lesions are innumerable and of extreme severity, but the visceral and nervous lesions are exceptional. It is the opinion of Lacapère that the impregnation of the individual by alcohol creates in the European permanent hypertension, which is necessary for the production of sclerotic processes. This hypertension is lacking in the Arab because of the complete absence of alcohol and, moreover, because he is usually suffering from malaria, which is known to tend toward hypovascular tension. The author has never observed sclerotic tuberculosis among the Arabs and, as a rule, the syphilitic infection of the tuberculous individual intensifies the tuberculous process, whereas in the European the opposite is sometimes observed. In his opinion, tabes and paresis are practically non-existent among the natives.

Syphilitic Elephantiasis of the Scrotum. Two cases of elephantiasis of the male external genitalia were observed by Levy-Bing and Gerbay.⁷ Elephantiasis of the scrotum occurs not infrequently as a result of late syphilitic lesions in the region of the external genitalia. The occurrence of elephantiasis as the result of a primary lesion, however, is much more rare. The first patient was a soldier 26 years old who developed two chancres of the scrotum which for some time went unrecognized. He had also blenorrhagia, which he had contracted at the

(5) Practical Medicine Series, 1918, Vol. VII., p. 192.

(6) Presse méd., July 3, 1919.

(7) Ann. des mal. vén., October, 1918.



Varioloform syphilis eruption of second attack.



Eruption on thigh; scar of old chancre on glans; second chancre on foreskin over corona.—J. F. Schamberg, page 187.

same exposure. About two weeks after the onset of the two chancres the scrotum became markedly edematous and infiltrated. A correct diagnosis had not been made when he came under the observation of the authors about six weeks after the onset of the chancre. By this time he had also developed a roseola. Spirochetes were found in the chancres and the Bordet-Wassermann reaction was strongly positive. The scrotal condition yielded promptly to intravenous medication.

The other case occurred not as a condition secondary to chancre, but as the primary condition itself. The patient was a Senegalais, 22 years old, who first noticed an edema of the penis and scrotum which gradually enlarged. Five weeks after the onset he came under the care of the authors who found the scrotum and penis markedly enlarged, with much thickened skin which suggested that of the elephant. The testicles and epididymes appeared normal. Being a Senegalais, their first thought was that it was elephantiasis due to filaria, and a careful search was made for these organisms in the blood, with negative results. The Bordet-Wassermann reaction was strongly positive, and after a series of intravenous injections the patient made an uneventful recovery.

Syphilis of the Epididymis. After a review of the literature and a study of seven personal observations, H. E. Michelson^s concludes that, contrary to the belief of many, syphilitic involvement of the epididymis is not an extremely rare occurrence, and will be more frequently found, if looked for. Bilateral involvement is unusual. The more common type encountered is the chronic diffuse interstitial type. The author finds that some cases of hydrocele are due to syphilis and that all patients presenting themselves for disease of the scrotal contents should be carefully examined for syphilis. The diseased portion is not necessarily confined to the upper pole, the entire epididymis being frequently involved.

Late Syphilitic Ulceration of the Face of Northern Africans. A great number of natives of Algiers present extensive ulceration and destruction of the center of

(8) Jour. Amer. Med. Ass'n., Nov. 8, 1919.

the face and this has led Lacapère⁹ to group these cases and to make a study of them. It is an interesting fact that the ulcerations tend to appear in a circle first described by Sabouraud as the location of predilection of the seborrheic lesions of the face. The reason for the location of the ulcers in this region is probably due to the fact that the resistance of the tissue within this circle is less than that of the rest of the face. The skin is covered with voluminous sebaceous glands, and the presence of the cartilage of the nose and of the mucocutaneous junctions of the mouth and nose make this region more vulnerable. The second reason is that the exposure of the face to the strong sunlight leads to premature senility of the skin of this region.

An interesting observation in these cases is the multififormity of the lesions in an individual. In the European, who receives early treatment, the late cutaneous lesion will usually be of one type. In the Africans, however, the absence of treatment leads to an unhindered progress of the disease and the co-existence of various types of lesions with extensive destruction of the tissues. The progress of the process takes place in several stages. It begins with infiltration, subsequent ulceration and, finally, healing. The whole process is very slow and years are required for cicatrization.

Severe Epistaxis Due to Unrecognized Gumma.

When an unusual change occurs in the nose, the pharynx or the larynx one should always think of syphilis. Mounier¹ saw a man who was having a very severe nasal hemorrhage which, at the time, seemed to be of ordinary origin. After he had removed the tampon he could find no apparent source of the hemorrhage. He put in a tampon and an hour later the patient returned bleeding more than ever. All the ordinary methods used for stopping hemorrhage were without effect. Owing to the possibility of cerebral complications, Mounier did not use chromic acid. The hemorrhages continued for a period of eight days and were so abundant that as a rule the tampons were gradually forced out. It was not until the eighth day that the author went into the history

(9) *Ann. des mal. vén.*, August, 1919.

(1) *Ibid.*, July, 1919.

thoroughly, at which time he found that there was a definite history of syphilis. He immediately put the patient on injections of mercury, and almost at once there was a lessening of the hemorrhage and a diminution of the pain in one of the eyes, from which the man had suffered intensely. After the fifth day the hemorrhage ceased and there was no further trouble.

As a rule, gumma in this region leads to an erosion of a vessel and hemorrhage which is usually preceded by marked headache, and associated with nasal mucopurulent secretion and vertigo. All of these symptoms, however, were absent in this case.

The Differential Leukocyte Count in Syphilis. Blumberg² is of the opinion that a differential white cell count is of diagnostic value in syphilis. The presence of syphilis is indicated by increase in the large lymphocytes. The differential count was not in any demonstrable manner affected by arsphenamin medication, except that there occurred an increase in the polymorphonuclears in cases in which the Bordet-Wassermann reaction was positive when the treatment was begun.

CENTRAL NERVOUS SYSTEM.

Inequality of the Pupils Early in Syphilis. In a study by Nicolau,³ of Bucharest, attention is called to a phenomenon which he has frequently observed early after the development of the chancre. This phenomenon consists in the inequality of the pupils which in order to be detected must be carefully searched for. The inequality of the pupils may develop so early after the infection that it precedes the roseola, or it may develop late in the infection and be followed by late manifestations of involvement of the central nervous system. The author finds this phenomenon so frequent in recent syphilis that he is very much surprised that other observers have not reported the findings before. This inequality of the pupils is not to be confused with the Argyll-Robertson pupil. It is quite independent of that but frequently is a precursor of the latter. The author

(2) Amer. Jour. Syph., October, 1918.

(3) Ann. de dermat et de syph., September, 1919.

recognizes the fact that inequality of the pupils may exist in the absence of syphilis. He has observed it in some families in which syphilis could be excluded, but he insists that it is a rare finding in the absence of syphilis.

In order to test this, he examined very carefully 200 soldiers in whom no evidence of syphilis could be found and encountered an inequality only seven times. Moreover, he recognizes the various causes for inequality of the pupil due to local pathologic changes, such as cicatricial deformity due to iritis, or to paralysis of the third nerve, or acute meningitis of tuberculous or other origin.

Nicolau attaches a great deal of importance to the technique of examination for the determination of the inequality of the pupils. The patient should be placed in a moderately dark room and the light should be very bright, preferably that of an electric light of high candle power or a pocket flash. The light should be placed squarely in front of the patient and he should be asked to fix his gaze on a certain object and keep it there. The inequality may not manifest itself at first but after exposure to the light for thirty seconds or more one of the pupils will show a tendency to relax, and this tendency to relax results in the inequality in which the author is concerned.

In about 10 per cent. of these cases of anisocoria the dilatation exceeds approximately $1/5$ to $1/4$ of the diameter of the normal pupil. In these cases the differences are so great that they are immediately evident. In about 70 per cent. of the cases the differences are definite but slight and are easily recognized by a careful observer. In the remaining 20 per cent. of the cases the differences are so slight that only after a considerable experience on the part of the examiner is it possible to detect the inequality. The phenomenon of inequality of the pupils is entirely independent of the loss of the light reflex peculiar to the Argyll-Robertson pupil. The unilateral mydriasis appears to be the expression of a relative loss of tonus of the sphincter. Under the stimulus of the light the pupils contract, but owing to the loss of tonus of the muscle it gradually relaxes.

Of seventy-five cases of syphilis in the primary period

the inequality of the pupils was found in twenty-two cases. All of these cases were in the "second incubation period" and presented nothing but the chancre and the regional adenopathy. Of these twenty-two cases, eight showed the phenomenon in the fourth week, seven in the fifth and four in the sixth. The author then reports in detail three cases in which he was able to fix exactly the date of the appearance of the phenomenon.

Examination of 409 cases of secondary syphilis showed that the inequality of the pupils existed in 153. The spinal fluid of 113 cases was examined in the secondary period and of these there were forty-three cases showing inequality of the pupils. Of the forty-three cases thirty-three showed a pathologic cell count.

An examination of sixty-eight cases of late syphilis in which there was no finding of involvement of the central nervous system, but in which there were cutaneous and mucous membrane lesions, revealed the inequality twenty-five times. In none of these twenty-five cases did the Argyll-Robertson pupil exist. The evolution of the pathologic cell count and the inequality of the pupils will not be found to be parallel. As a rule, the lymphocytosis early in syphilis will disappear except in very rare cases, whereas the pupillary inequality, once it has appeared, constitutes an indelible stigma.

This inequality is not necessarily a bad prognostic sign, but it constitutes a menace for the future of the patient and should be carefully watched. It should serve as a valuable sign to indicate to the physician the need for very close watching over the future of the syphilitic.

Syphilis of the Central Nervous System in Natives of Algeria. Last year Montpellier showed that, contrary to the belief of many men, syphilis of the central nervous system occurs in the natives of Algeria in about the same proportion of cases as in the European races. This year Montpellier⁴ reports another series of spinal-fluid examinations made on the same race of people. The cases occurred in people in the ordinary walks of life, who had not been subjected to any unusual mental strain. There was no indication of chronic alcoholism. The

(4) *Ann. des mal. vén.*, January, 1919.

average age was 33 years, and most of the patients were unaware of the existence of any nervous involvement.

The Cerebrospinal Fluid in Herpes Zoster and the Relation of the Disease to Syphilis. During the treatment of a large number of cases for syphilis with arsphenamin it was noticed that many cases of herpes zoster occurred. An attempt was made by Brown and Dujardin⁵ (a) to determine whether there was any change in the cerebrospinal fluid in cases of herpes zoster; (b) whether there was any relation between syphilis and herpes zoster and, (c), whether there was any relation between arsphenamin injections and the development of herpes zoster.

In forty-two cases the cytologic estimation was made but the results were not uniform. In twenty-eight cases there was some degree of lymphocytosis and this varied from one cell to 470. In ten cases the counts registered more than 50. There was no relation between the cell count and the intensity of the eruption, but rather the reverse. A determination of the albumin in the spinal fluid was carried out by Sicard's method. No constant change was found but in the majority of cases there was a slight increase. Only in one case was the globulin reaction definite, and this occurred with a cell count of 350. The Bordet-Wassermann reactions on twelve cases of herpes zoster were all negative; two of the patients had had syphilis with adequate treatment. In a series of 1,200 cases of syphilis in many stages, nine cases of herpes zoster developed, making approximately 4 per 1,000 *per annum*. Among 13,000 other cases only ten cases of herpes zoster were seen, which makes less than 1 per 1,000 *per annum*. It would seem, therefore, that there is a predisposition to herpes zoster in syphilitic subjects.

TREATMENT.

Treatment of Syphilis in the French Army During the War. Without being able to give figures, Laredde⁶ says that the number of officers and men who acquired

(5) Brain, 1919, Part 1.

(6) Bull. Soc. franc. de dermat. et de syph., 1919, No. 1.

syphilis during the war reaches the hundreds of thousands. Moreover, the number of women already contaminated; those women who have miscarried; those infants with congenital syphilis already dead; those living a very precarious existence, and those who will be born within the next few years are still more numerous. The wounds and the suffering which were the immediate effect of the war perhaps are not to be compared with those which were incidental and which arose from contagious diseases propagated by war conditions. It is well known that tuberculosis caused terrific mortality among mobilized soldiers, but syphilis probably, in Laredde's opinion, has caused even greater suffering and mortality.

Laredde is very caustic in his criticism of the instructions given by the War Department for treating syphilis which had been acquired prior to the outbreak of the war and which presented no active manifestations. These patients were to be treated with internal medication. In order to care for venereal diseases there were created venereal centers having all the necessary clinical and laboratory facilities for the management of venereal cases. The instructions of the medical department required that patients should be sent to these venereal centers who came under the following classifications:

1. Every patient with a typical chancre, or with a simple erosion which might be a suspected chancre.
2. Every balanitis or balanopositis suspected of being syphilis.
3. Every case of secondary syphilis accompanied by contagious lesions.
4. Every case of syphilis with secondary manifestations, however mild.
5. Every case of syphilis which had resisted treatment and which had not been treated in an intensive manner by intravenous methods.

The object of these instructions was (1) to cause to disappear in a minimum time all primary and secondary manifestations of syphilis; (2) to sterilize in the shortest possible time all sources of contagion; (3) to return the men to active service as quickly as possible. All of which means that the hospitalization of the patient should

be minimized in order that the fighting strength should be maintained.

Laredde criticises these provisions of the medical department because, in his opinion, the object was not to treat syphilis in a way that would result in permanent cures, but merely to temporize by rendering the patients non-infectious.

In 1918, the author observed eighty-seven syphilitics who had acquired their infection between 1913 and 1916. Of these twenty-three had treated themselves, following the recommendations of the political journals, or had been treated at irregular intervals in public dispensaries. Of twenty-six cases infected in 1913-14 and '15 he was able to get exact details of twenty-three. Of a total of twenty-six cases in 1918, seventeen had a positive Wassermann reaction and eight had contagious mucous membrane lesions. Of another group of thirty-eight cases infected in 1916 and studied in 1918, twenty-seven had positive reactions, only nine negative reactions, and nine cases presented contagious lesions of marked activity. In not one of these cases had the ministerial instructions relative to treatment been carried out. This leads the author to suspect that a large number of the men who have been infected during the war have not been properly treated. Moreover, most of those men are contagious without realizing it. The result has been that a terrific epidemic of syphilis was not averted as it would have been had the instructions been carried out.

In the discussion which followed the reading of this paper before the society many men criticized Laredde very severely. Milian said that his statements were fantastically exaggerated. During the years following the formation of the venereal centers they treated from 1,000 to 1,500 syphilitics yearly, of which probably one-third were old cases. This would make for the ten armies about 5,000 new cases of syphilis for the army at the front, a figure which would not be more than the number for a civil population of equal size. More cases than that are seen at one consultation in the St. Louis Hospital in peace time.

Gougerot protested against the assertion that the syphilitics were not properly treated in the army. He

said that physicians had full liberty and every facility for the proper management of cases, which was set forth in Circular 251. He thought it was inexact and unjust to accuse the *Sous-Secrétariat* of having given superannuated instructions for the care of syphilitics. If, as indeed may have happened, in individual cases certain patients were not well cared for, this was the fault of the individual physician in charge, and the individual errors should not be charged to the organization. The soldiers were very much better cared for in the army than they had been in civil life in most of the cities of France.

Brocq stated that in 1915 he and Thibierge had been consulted by the *Sous-Secrétaire d'Etat* concerning the best methods of treatment of syphilis in the army. They had advised the use of arsenobenzol and of luargol, and from that time on these arsenical preparations had been recommended in their ministerial circular. He was inclined to agree with Laredde concerning the number of new cases of syphilis. In his own service from June, 1917, to December, 1918, there had been 2,855 cases. Therefore there has been an incontestable increase.

Chatin believed that inasmuch as all the men from 19 to 48 years had been reclassified that probably accounted for the apparent increase of syphilis in the army.

Treatment of Antenatal and Postnatal Syphilis. At the Thavies Inn, venereal center for pregnant women, John Adams⁷ has treated thirty cases of pregnant syphilitic women. On admission a Wassermann test is made on the blood of every patient admitted. Immediately on the birth of the child a specimen of blood is taken from the vessels of the divided umbilical cord in a cubic centimeter glass tube, and a similar amount of the mother's blood is secured for the purpose of a Wassermann test. A small portion of the placenta is also obtained for examination for spirochetes. As soon as syphilis is diagnosed in the mother, treatment by arsphenamin is commenced, and weekly doses are administered by intravenous injections of grey oil. Pregnant women bear intravenous injections of salvarsan extremely well, and the injections can be given up to the

(7) Brit. Med. Jour., Nov. 16, 1918.

time of confinement. The arsphenamin preparations have been galyl and novarsenobillon; galyl in glucose solution was used exclusively for the babies. In the case of mothers weekly injections of a small dose are given and gradually increased until nearly the maximum is given. Intramuscular injections of mercury are given in 1-grain doses on the same day as the arsphenamin is administered.

In the Thavies Inn center every dose given to mothers and babies is registered on a chart for future reference, and the weekly weight of the baby is noted.

It is found most convenient to give the intramuscular injections, both of arsphenamin and mercury, with a special syringe graduated in fortieths of a cubic centimeter. Thus, each division of the syringe corresponds to 1 cg. of mercury. For the purpose of sterilization the needles should be made of platino-iridium, which can be heated in a flame without damaging the point. When galyl in glucose is used the needle must be carefully wiped and water passed through the needle two or three times before heating it in the flame, as a high temperature on glucose causes it to solidify and renders the needle unfit for use.

Even in the weakest, premature syphilitic baby the writer has never seen anything approaching a local inflammation following an intramuscular injection of galyl or mercury, neither do the injections appear to cause pain. The babies' stools are usually grass green for a day or two after the injection of galyl, but there is not other evidence of digestive disturbance.

It was difficult at first to determine what dose of arsphenamin the babies should be treated with; to give an intravenous injection to a baby from 2 to 7 days old is usually impossible. There is a preparation of galyl in glucose which is admirably suited for the purpose of intramuscular injection. A new-born baby is about one-seventeenth the weight of the mother; the average dose of galyl for an adult is 0.30 g., one-seventeenth of that quality would be about .002 g. This should be gradually increased up to .05 g. or more as the child grows and it is borne very well. The mercury is given in doses of from

1/4 to 1/2 grains or more, corresponding to .0013 to .003 g.

The safest and most convenient way to give intramuscular injections to new-born babies is the gluteal region, and if a line be taken from the anterior superior spine of the ilium to the commencement of the gluteal fold and this line divided into three sections, anywhere in the middle third is the region to select. The intramuscular galyl and mercury injections can be given the same day on opposite sides, and are well-borne. It is advisable that there should be an interval of a week or ten days before repeating the injections.

Out of thirty cases, six babies have been born free from any evidence of syphilis, although the mothers have still given positive reaction for a considerable time after delivery.

It has been found that those babies who have at first a positive reaction generally yield a negative reaction after treatment sooner than their mothers. Up to the present there has been no case in which a baby who had become negative has later developed a positive Wassermann reaction. The average number of doses of galyl required to bring about a negative reaction has been 65 and the amount per case .026 g. With one exception it has been found that the child gained regularly in weight and showed no further signs of syphilis.

The wastage of child life due to syphilis is terrible. Dr. Routh, estimated that 27,000 deaths in England and Wales alone occur annually in the antenatal period and the week following birth as a result of syphilis and Dr. Russell Andrews in his evidence before the Royal Commission on Venereal Diseases stated that nearly 50 per cent. of all syphilitic fetuses are stillborn and that 75 per cent. of those born alive die within the first year; most of these deaths occur during the first week of life.

Intensive Arsphenamin Therapy. Very soon after the intravenous method began to supersede the intramuscular method of administration of arsphenamin, some of the Viennese workers attempted to give large doses at frequent intervals. This method was soon abandoned, however, because of the unfortunate results which

were probably due in great part to the toxicity of the German product.

About two years ago Pollitzer⁸ revived interest in this method, by showing that if the cases be properly selected, and the dosage not too large, this form of treatment is of great value.

Hazen⁹ reports the results obtained by him in a series of cases. In all he gave ninety-eight injections to twenty-two patients. Each patient received at least three injections and some as many as eight, usually at seventy-two hour intervals. In all of these cases there occurred no untoward result. Whereas a few cases gave rather severe reactions such as vomiting, diarrhea and headache, there was no indication of any increase in intolerance to the drug. Albumin was not found at any time although searched for carefully after each injection, nor did jaundice occur in any of the cases.

The clinical results were very good. Nineteen of the cases showed positive Bordet-Wassermann reactions at the time the intensive treatment was instituted, and in all the cases the reaction became promptly negative with two exceptions; in one case three series of three injections were necessary, and one patient disappeared from observation after the first series.

The preparation used was in all cases the arsphenamin prepared by the Dermatological Research Laboratories of Philadelphia, and marketed under the name of "Arsenobenzol." The dosage was maintained at 0.4 gm. per 150 pounds of body weight, dissolved in distilled and boiled water.

[As noted in the editorial comment in these volumes we have been using the method of treatment since it was first advocated by Pollitzer. With it we have been able to clear up positive reactions which had resisted the older methods for months. Moreover, we have found it to be of the greatest value in the treatment of primary and secondary syphilis, as well as in the late cases in which there is a persistent Bordet-Wassermann reaction.—M.]

(8) Practical Medicine Series, 1916, Vol. IX., p. 194.

(9) Amer. Jour. Syph., October, 1918.

Clinical Study of the Rectal Administration of Arsphenamin. The administration of arsphenamin by rectum was first studied in 1912. Bogrow of Moscow prepared suppositories of cocoa butter containing from 0.1 to 0.2 grams of arsphenamin. Weill, Morel and Mouriquand used suppositories of glycerine. Geley was the first to utilize enteroclysis. Lelong also made use of this method of treating both hereditary and acquired syphilis. The technique was very simple, and consisted of preparing arsphenamin in salt solution as for intravenous injection, diluting it with an equal amount of salt solution, and injecting it high into the rectum. The injection was preceded, of course, by a cleansing enema. Various other men adopted the method and finally Rajat studied in detail the treatment of 125 cases of syphilis treated in this manner. Rajat used the rectal injections because he was of the opinion that intravenous injections were too dangerous.

Azémar¹ of Audry's clinic in Toulouse has made a careful clinical and chemical study of the therapeutic results in active syphilis and of the elimination of arsenic in the urine in both intravenous and rectal injections of arsphenamin. The patient was prepared for the injection by a very light repast the night before, and a cleansing enema before the rectal injection. The drug was dissolved either in physiologic salt solution or in distilled water. To this solution was added from 10 to 15 drops of tincture of opium and the whole was brought to body temperature. Not more than enough water was used to dissolve the neo-arsphenamin. This was then injected with a glass syringe of from 25 to 50 centimeter capacity. Care was exercised not to inject any air, because if this occurred expulsion of the solution was likely to result. The best time to give the injection was found to be early in the evening, because the patient could then remain quietly in bed over night. The optimum dose of neo-arsphenamin was found to be about 0.9. The interval between injections was determined by studying the elimination of the arsenic in the urine, and it was found that the patient could be kept saturated by giving a rectal injection every six days. Study of the elimination

(1) *Ann. de dermat. et de syph.*, September, 1918.

of arsenic showed that it first appears in the urine in two hours after the injection; that it slowly increases until the third day, and thereafter gradually decreases to the fifth. By the sixth day the arsenic has disappeared from the urine. It was found that the elimination of metallic arsenic in the urine is extremely variable, not only with different individuals, but also with different injections in the same individual. One mucous membrane will vary considerably in its co-efficient of absorption from another. The elimination of arsenic, however, is, as a rule, directly proportional to the amount injected. In order to compare the results of the rectal administration of neo-arsphenamin, the elimination of arsenic in the urine was also studied after intravenous injection. It was found that the arsenic appears in the urine within one hour after intravenous injection, increases to the third day, and gradually decreases to the eighth day; it may in some cases be perceptible on the tenth day, and in only one case was it found on the fifteenth day.

The author concludes that the rectal administration of neo-arsphenamin is efficacious, easy and simple. It has the advantage of not necessitating any medical intervention, and could be administered by almost anyone if the solution had been properly prepared. The therapeutic results, however, are less rapid, less lasting and less constant than those following the intravenous method. The method can be used in children and in subjects lacking proper veins, or having veins that have been occluded by previous intravenous injections.

Injection of Spinal Fluid Intravenously. Believing that the toxin elaborated in the peculiar constituents of the cerebrospinal tract differs from the toxin formed in somatic syphilis, and that the antibodies produced against a systemic syphilis are not specific against a "nerve-derived toxin," led by J. B. Gooken,² to inject spinal fluid intravenously in the hope that this would stimulate the production by the blood of antibodies which are specific against the toxin, and which are found only in the spinal fluid. These intravenous injections are combined with the intraspinal injections of arsphenamized and mercurialized serum. A positive chemo-

(2) Amer. Jour. Syph., October, 1918.

taxis is thereby created toward the spinal canal, resulting in the carrying of the antibodies which have been developed in the blood by the spinal fluid, into the spinal canal, and the entrance of these antibodies into the spinal canal will be facilitated by the increased permeability of the meninges following the aseptic inflammation set up by the intraspinous injection of the patient's serum.

Daily inunctions of mercury are given during the entire course of treatment. At the end of fifteen days this is supplemented by weekly injections of arsphenomized serum, to which has been added 1/50 grain of mercury benzoate dissolved in 1 c.c. of normal saline. The spinal fluid which has been withdrawn before injecting the serum is then injected into the vein.

The author states that a comparison of the results obtained with this method with those of the intraspinous method alone shows that three of these treatments gave a serologic improvement equivalent to that of six of the Swift-Ellis treatments.

Vasodilators in the Intravenous Treatment of Syphilis with Arsphenamin. Introduction of vasodilatation for the purpose of facilitating the introduction of the needle into the vein, and also to increase the permeability of the tissues to arsphenamin is suggested by G. B. Barnes.³ By the action of vasodilators the arteries and capillaries are opened up so that the blood impregnated with arsphenamin can be driven into the more remote tissues and the lymphatic channels can be more thoroughly reached. The value of any vasodilator for this purpose must be determined by the extent to which it accomplishes this result. The vasodilator which seems to be the best for the purpose considered, is nitroglycerine. Although its action is rather fugacious, it seems to open up the circulatory channels most thoroughly. However, the fact that its action is, especially in some people, of short duration may be an important point in its favor, for it can be applied during short periods at various intervals; and by giving repeated doses in close succession its effects can be, whenever desired, prolonged. Careful attention should be given to proper dosage. Of course, any patient who experiences

(3) Boston Med. and Surg. Jour., May 15, 1919.

the so-called nitritoid reaction should not be given vasodilators until that reaction has passed off. Furthermore, every patient's response to arsphenamin should be ascertained before vasodilators are given at all.

[With the exception of those patients who have had their veins obliterated by unskilled hands, we rarely encounter an arm which causes any difficulty in giving the injection. Owing to variations in the different preparations of arsphenamin, and the variation in different lots of the same preparation no one is able to predict when the reaction will occur, and therefore to take chances in increasing the vasodilation due to arsphenamin by giving nitroglycerine would be extremely unwise. The therapeutic advantage to be gained is extremely doubtful.—M.]

Intravenous Injections of Arsenious and Mercuric Iodides. Soon after the outbreak of the war when it became evident that supplies of salvarsan would be increasingly difficult to procure, Splittel⁴ set about experimenting on syphilis and yaws with various preparations of mercury, iodides, arsenic and antimony in common use, taking as a working hypothesis dosage to the point of tolerance by the intravenous route. He soon became convinced that the drugs contained in Donovan's solution lent themselves best to this form of treatment.

The injection will be found to produce effects on syphilitic lesions, whatever their stage, little short of those obtained with salvarsan and allied products. In three and a half years the author has given over 5,000 of these injections in syphilis and yaws. In syphilis and in yaws the formula given below may be used without modification:

The solution is made up in the following way: It has to be rendered *slightly alkaline*, and this is best done by first adding to it 20 minims of 0.5 per cent. solution of phenolphthalein, and then neutralizing by carefully adding a 25 per cent. solution of sodium hydroxide. When alkalinity is reached the solution begins to assume a pink color owing to the presence of phenolphthalein, which thus serves both as an index of correct alkalinity

(4) Practitioner, 1919, p. 212.

and as a coloring agent. Once the neutral point is reached the alkali is cautiously added drop by drop until a distinct pink color is obtained. If thought necessary, glazed litmus paper may be used as a control of alkalinity, but phenolphthalein is much the more delicate index. It is important that the solution should be only slightly alkaline; if too alkaline, a precipitate results either immediately or after some hours or days, and the efficiency of the solution is impaired. Should the color fade on keeping, it means that it has become too acid (due probably to the presence of hydriodic acid); in which case dilute alkali should be added until the original pink color returns. The solution keeps well for several weeks, and if stored in a glass-stoppered bottle under aseptic precautions may be drawn upon for injection without subsequent re-sterilization.

In an emergency, a very efficient injection may be made out of ordinary Donovan's solution, which was the first solution used in earlier experiments. Donovan's solution is diluted with an equal quantity of sterile water; it is then rendered slightly alkaline by adding a 15 per cent. solution of sodium hydroxide while testing with litmus paper. The dose of this is from 7 to 12 c.c. for intravenous administration. Its disadvantage is that it contains too much mercuric iodide, and is likely to cause much salivation if caution be not exercised.

The solution now used as a routine is as follows:

Mercuric iodide	3 24
Arsenious iodide	2 59
Sodium (or potassium) iodide.....	28 42
Distilled water	1000

From 8 to 15 c.c. is the dose for an adult. The dose should be small to begin with and gradually increased according to tolerance. From four to six injections at intervals of from four days to a week constitute a course. Several such courses should be given, with intervals of a month or six weeks between them.

The injection is administered with a 20 or 30 c.c. glass syringe, into which the required quantity of solution is drawn; the syringe is then filled up to its full capacity with sterile water. This further dilution is necessary to

obviate the slight phlebitis that is otherwise apt to ensue, rendering future injections into the same vein difficult.

The reaction depends on the dosage employed; it is negligible and evanescent if the dose is graded to tolerance. Heart and kidney disease are no contraindication to cautious dosage. One or more of the following symptoms may be produced within a few hours of injection: Chill, fever, malaise, headache, vomiting, pains, and burning sensation in the body. Later effects are gingivitis and salivation, coryza, lachrymation, diarrhea and griping.

Calomel Inunctions. Last year⁵ Schamberg reported the results of his experimental work with calomel inunctions. Inasmuch as blue ointment is so uncleanly and therefore leads to detection, and moreover is very irritating, the use of calomel ointment was welcomed.

Cole and Littman,⁶ however, made a clinical study of the efficacy of calomel in fifty cases of florid syphilis and were convinced that calomel inunctions are almost totally inefficient against primary and secondary syphilis. The inunctions very rarely produce salivation or gingivitis. This means poor absorption of the mercury and explains this clinical inefficiency. The inunctions may occasionally produce dermatitis. These results have led the authors to abandon calomel inunctions, and they strongly advise against their further use in the treatment of syphilis.

TOXICITY OF ARSPHENAMIN.

Toxicity of Neosalvarsan. A great deal has been written in times past concerning the toxic reactions following arsphenamin injections. Theories advanced concerning the cause of these reactions have usually fallen into one of three categories: first, the technique of the injection (mechanical toxicity), or, second, the toxicity of the water, or the salt solution used in diluting the drug.

Another theory is now advanced by Golay⁷ of Geneva, who believes that a great deal of the toxicity of the neo-salvarsan is due to small amounts of the solution

(5) Practical Medicine Series, 1918, Vol. VII, p. 226.

(6) Jour. Amer. Med. Ass'n., Nov. 8, 1919.

(7) Ann. de dermat et de syph., September, 1919.

adhering to the glassware and being carried from one injection to another. It is well known that neo-arsphenamin is rapidly oxidized in the air and when this oxidation product is injected the toxic symptoms may be very severe. Inasmuch as neo-arsphenamin is usually given in highly concentrated solutions, one drop of the solution after oxidation has taken place may contain a large quantity of the drug, enough to cause very severe toxic symptoms.

Golay found that nitrate of silver solution is a very delicate reagent for detecting minute traces of neo-arsphenamin. In a 1 per cent. solution of neo-arsphenamin silver nitrate gives an abundant precipitate of brownish-black or violaceous-black precipitate, according to the quantity of silver nitrate used. In a solution of 1/10,000 of neo-arsphenamin the silver nitrate causes a marked brown-violet coloration. The author found that having washed the syringe used in giving the injection four or five times the wash water of the fifth time in the presence of silver nitrate gave a reaction which corresponded approximately to a solution of 1/100,000 of neo-arsphenamin which, if thoroughly oxidized, might, in susceptible patients, be quite toxic. He advises very thorough washing of all the glassware and syringes used between injections.

[The studies of Schamberg and others have fairly well demonstrated the fact that the toxicity of arsphenamin is almost entirely due to the preparation itself, assuming, of course, that freshly distilled water has been used. With ordinary care in washing graduated cylinders and syringes very little need be feared concerning toxicity of traces of oxidized neo-arsphenamin being carried over from the last injection.—M.]

Toxicity of Certain Lots of Arsphenamin. Much effort has been expended in attempts to fix the cause of the toxicity of salvarsan. Most of the earlier efforts were directed toward eliminating the toxicity of the water, or attempting to fix on the size of the dose or the number of injections as the causative factors. In our own work⁸ we found given control numbers of the old

(8) Ormsby and Mitchell: Jour. Amer. Med. Ass'n., Dec. 9, 1916.

salvarsan were particularly toxic and some of these were obliged to return to the agents. This paper was published in 1916. Since that time many observers have noted that preparations of given control numbers were particularly toxic.

Lacapère⁹ found that a certain lot of tubes containing 0.45 gm. novarsenobenzol (the maker is not mentioned) was all toxic and led to severe nitritoid crises. Later two deaths occurred from the use of these same tubes in Morocco, where he was stationed. In order to determine the toxicity of a given lot, Brocq has adopted the practice of dividing a tube containing 0.9 gm. of the novarsenobenzol to be tested between a number of patients. In the absence of a number of patients who can be treated in a given time, Brocq gives 0.1 gm. of the preparation to a patient and waits for an hour or more to elapse. If no reaction has occurred he feels safe in giving the full dose indicated.

In the discussion which followed the presentation of this paper, a number of men gave their experiences, which seemed to coincide with those of the writer. Laredde, however, disagreed with all the others, as usual. In his opinion practically all the accidents are due to excessively large doses or to the Herxheimer reaction.

[Since Schamberg has made his preparation available for clinical use, we have used it in our private practice almost exclusively. Occasionally at first some of the tubes were proved to be toxic, but with time this toxicity has gradually decreased until now it is a great rarity, especially the immediate or nitritoid reaction. Occasionally a patient complains of slight nausea and diarrhea. We have had abundant opportunities of demonstrating the lack of toxicity of the preparation inasmuch as we have been giving injections in series of three, allowing only one day to intervene between injections. The dosage, however, has never been above 0.4 of the original arsphenamin. In our opinion Laredde is justified in maintaining that the dosage is frequently too large and leads to untoward results.—M.]

Severe Nitritoid Crisis. A very severe reaction following the injection of arsphenamin of the neo-arseno-

(9) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

benzol type in a woman 27 years old, who had had a number of injections prior to the severe reaction, is reported by Tzanck.¹ The treatment was begun during the period of the roseola, during which time she had weekly injections. Persistent headache, however, supervened and a lumbar puncture was made. This disclosed a moderate degree of meningitis and a series of four more injections of neo-arsphenamin was given. She was then put upon intramuscular injections of grey oil. Meanwhile, an acute salpingitis occurred in 1919 which confined the patient to bed for three months. Thereafter she was given more grey oil, but because of the pain she requested arsenical medication. The first dose consisted of 0.15 g. and about a week later another injection of 0.10 g. of novarsenobenzol (Billon) was administered. There was an intense reaction immediately after the injection had been given. The patient lost consciousness and artificial respiration became necessary. Adrenalin was administered subcutaneously and by mouth. The circulation was so sluggish that the subcutaneous injection of adrenalin caused necrosis of the tissue.

The interesting points in this case are that a patient who had tolerated doses ten times as great on previous occasions reacted so severely to this small dose. The question of the toxicity of that particular control number is eliminated because the author had given injections to a great many patients from this same lot. He is of the opinion that the intercurrent salpingitis might have so altered the adrenals that the tolerance of the patient for the drug was lost. He had been tempted to give the patient a large dose of adrenalin and follow it with a very small dose of arsphenamin, but felt that the possibility of fatal outcome did not justify him in making the attempt purely for scientific purposes.

Death Following Injection of Arsphenamin. The death of a girl 19 years old following an injection of arsphenamin is reported by Sée.² The patient had received a number of injections prior to the one which caused her death without any symptoms which would suggest intolerance. After an injection of 0.45 g. of

(1) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(2) Ann. des mal. vén., June, 1919.

neo-arsphenamin she developed, during the night, an epileptic seizure which, according to her friends, had occurred on occasions not in any way associated with intravenous medication. The patient fell into a deep stupor from which she could not be aroused, despite the administration of adrenalin, and death finally supervened.

[The possibility of attributing a reaction to an intravenous injection, when the reaction was merely a coincidence, is well illustrated by a case seen at Rush Medical College. A solution of arsphenamin containing enough for four injections was prepared in the usual way and three of the injections were administered. The fourth injection was given to a man who had received on previous occasions some six injections without manifesting any signs of intolerance. Immediately following the withdrawal of the needle the patient began to complain of intense pain in the head and in the epigastrium. He developed strabismus and rigidity of the muscles. He was immediately sent to a ward in the hospital and placed in bed. His wife was sent for because it was suspected that he would probably die. By the time she had arrived, however, he was apparently normal and his wife explained that he had had on many occasions similar epileptiform seizures, and that if she had known what it was all about she would not have bothered to come to the hospital. Without the explanations of the wife this epileptiform seizure would have been put down as a very severe toxic reaction due to the intravenous injection, whereas it was merely a coincidence, or else the injection had merely served to set off an epileptiform attack.—M.]

Eclampsia and Coma Following Neo-arsphenamin.

An interesting case of eclampsia and coma following the second injection of 0.6 neo-arsphenamin dissolved in 10 c.c. of water is reported by Roblin.³ The patient was a young woman with a marked and typical roseola. She was given first a few injections of biniodide of mercury, after which she was given the first injection of arsphenamin. No symptoms of intolerance were observed and about nine days later the injection was repeated. Three

(3) *Ann. de dermat. et de syph.*, September, 1919.

days after the second injection the patient developed a high temperature with retention of urine. She was given adrenalin, caffeine and sparteine hypodermically. Within three days all the symptoms had passed and the patient left the hospital apparently in good condition.

Nitritoid Crisis after Colloidal Sulphur-Mercurial Injections. The nitritoid crisis occurring after arsphenamin injections was described some years ago by Milian and has been observed by everyone giving these injections at not infrequent intervals. A reaction closely simulating these nitritoid crises was observed by Levy-Franckel⁴ after the injection of a colloidal sulphur-mercury preparation. The patient was a young woman who had a series of arsphenamin injections followed by a series of biniiodide intramuscular injections, and at a later date a series of luargol injections. Following the luargol series she was again given intramuscular injections of mercury and manifested some signs of intolerance. She was given an intravenous injection of colloidal sulphur-mercury and immediately after the injection presented all the symptoms of nitritoid reaction. There was immediate hypersecretion of the mucous membranes, respiratory embarrassment and marked congestion of the face. Auscultation disclosed signs of bronchitis and a pulse of 100 was present. She was given adrenalin subcutaneously, as recommended by Milian for the nitritoid crisis after arsphenamin, and made an uneventful recovery. The author is unable to account for the toxicity of the drug, inasmuch as neither sulphur nor mercury is a vasodilator. The fact that hydrogen sulphid was eliminated in the urine led him to believe that this might be the toxic element.

Pneumonias Following the Injection of Arsphenamin. A series of nine cases of pneumonia developing immediately after the injection of arsphenamin (Schamberg) occurred at Fort Des Moines in November, 1918, and is reported by Schwerdtfeger and Tinker.⁶ Symptoms of pain in the chest, cough, dyspnea and prostration occurred during, or immediately after the injections. Examination of this particular lot of arsphenamin by

(4) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

(6) Amer. Jour. Syph., July, 1919.

G. W. McCoy, Director of the Public Health Service, showed that it was up to the standard of purity, and in his opinion the unfortunate results must have been due to the preparation of the solution for injection. Nearly 0.5 g. was given in 20 c.c. of water with a syringe.

[Those of us who adhere to the gravity method and to the higher dilutions, which have been shown by long usage to be safe, are not infrequently laughed at by those who pride themselves on their dexterity in the use of the syringe and the high concentration of arsphenamin solutions. However, we frequently have the opportunity of seeing arms which are indurated and which occasionally undergo sloughing as the result of syringe technique. It is entirely too easy to inject a quantity of very strong solution into the tissues before one is aware that the needle is not properly within the vein. High concentrations of arsphenamin are undoubtedly more toxic than the high dilutions and, moreover, a slight excess of sodium hydroxide in a small quantity of solution is much more destructive to the veins than it would be in a greater volume of fluid. Many veins are entirely obliterated and subsequent treatment is made extremely difficult because someone has been in too great hurry to use the gravity method, and to allow a reasonable amount of time for giving the injection. No physician is so busy that he is justified in lopping off five minutes from the time required for giving the injection to any patient. The future well-being and even the life of the patient may be sacrificed because the physician is in too great a hurry.—M.]

THE BORDET-WASSERMANN REACTION.

Standardized Technique for the Bordet-Wassermann Reaction. Proposals for the adoption of certain uniform methods of technique for the purpose of standardizing the Bordet-Wassermann reaction are made by Goubeau.⁷ He suggests that first an original Bordet-Wassermann should be carried out with a serum that has been inactivated at 56°, and with a standard antigen made from syphilitic fetal liver. As a control the reac-

(7) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

tion should be carried out with the inactivated serum as suggested by Halion and Bauer. Any other control tests that are carried out should be made simultaneously and should be merely controls. Another important point is the uniform method of recording results. Much confusion now arises because the methods of reporting results are not uniform.

Studies in the Standardization of the Bordet-Wassermann Reaction. The first paper giving the results of the experimentive work on the standardization of the Bordet-Wassermann is by C. P. Brown and J. A. Kolmer.⁸

The authors found that it is highly important to have all glassware used in the Wassermann reaction (pipets, test tubes and flasks, chemically clean and free of all traces of acid or alkali by reason of the marked antilytic (anticomplementary) and hemolytic properties of these substances.

Amounts of sodium hydroxide as low as 1 c.c. of a 1/400 dilution of a N/1 solution in 2 to 3 c.c. of fluid may be anticomplementary while 1 c.c. of a 1/100 dilution proves hemolytic; approximately 1 c.c. of a 1/500 dilution of N/1 solution of hydrochloric acid is anticomplementary and 1 c.c. of a 1/300 dilution hemolytic. Bichromate cleaning fluid proved anticomplementary in amounts as low as 1 c.c. of a 1/900 dilution and hemolytic in 1 c.c. of 1/600 dilution. *It is possible that minute traces of acid or alkali in the glassware may be responsible for falsely positive Wassermann reactions with normal serums;* large amounts may produce negative Wassermann reactions with syphilitic serums, probably by reason of the direct hemolytic activity of mineral acids and alkalies in amounts greater than sufficient to destroy complement.

The use of one pipet for measuring different serums in conducting the Wassermann reaction introduces the possibility of carrying over sufficient syphilitic serum into a normal serum to produce an erroneous result, unless the pipet is carefully washed between each serum. The use of a separate pipet for each serum is advisable.

Test tubes must be of a size suitable to the technique

(8) Amer. Jour. Syph., January, 1919.

in order to avoid a high column of fluid in a narrow test tube, which tends to interfere with hemolysis.

The size of the test tube depends upon the total volume of fluid in the technique employed; it is advisable to use a tube of such width that the height of the column of the contents is not too great as this factor alone introduces an error in the work by interference with hemolysis. In an experiment, an antishoop hemolysin was titrated with 1 c.c. of 1/20 complement and 1 c.c. of 2.5 per cent. suspension of sheep cells, in test tubes of two sizes; the correct unit of this hemolysin was 0.4 c.c. of 1/2,000 dilution whereas in a narrow tube (diameter 6 mm.) hemolysis was incomplete in this amount and particularly when the total volume was brought up to 5 c.c. with saline solution. This experiment is given to show practical importance of using test tubes of such diameter that the total volume will not be of a greater depth than 5 cm. in order to avoid a possibility of error. Furthermore, the diameter should be such that the contents may be thoroughly but gently mixed by rocking the tube instead of requiring capping with a finger and reversing several times. In the methods proposed as a standard technique, the test tubes are of rounded bottoms, with no lip and measure 8.5 cm. in length with an internal diameter of 12 millimeters (the walls are about one millimeter in thickness, which wear well).

Since the material in the Wassermann reaction is non-infectious it is unnecessary to sterilize the tubes and flasks by boiling after use as part of the cleansing process; furthermore, as a result of boiling the glassware repeatedly in soapy water (alkali), the glass becomes cloudy and unsightly. *It is highly desirable to use test tubes of uniform size which are physically and chemically clean, bright and glistening and preferably sterile; also to have this glassware set aside for use in the Wassermann reaction only instead of for general laboratory work.*

After use the tubes are emptied; rinsed in running tap water; washed inside and outside in a pan or bucket of warm soapy water; thoroughly rinsed in running tap water and placed upside down in metal baskets and

heated in a hot-air oven until a piece of fresh cotton placed in the oven has turned a light brown color.

It is unnecessary to plug each tube with cotton, although it is advisable to plug the flasks because of their use during subsequent work; in connection mention may be made of the report of Langer who found that cotton may contain antilytic substances and to warn against permitting blood, complement serum, or other reagents to soak into cotton stoppers by reason of the possibility of thereby dissolving out anticomplementary material. In some laboratories it is customary to boil the tubes in soapy water; rinse in tap water; immerse briefly in 1 per cent. hydrochloric acid to neutralize the alkali of the soap; rinse thoroughly and sterilize.

The boiling and immersion in acid are unnecessary as routine procedures, although it is occasionally necessary to do this with tubes which are spotted and particularly dirty; *the rinsing after immersion in the acid bath must be particularly thorough in order to remove all traces of acid.*

New test tubes should not be used until thoroughly washed with soapy water, rinsed and sterilized as described above. In some laboratories it is customary to give them an acid bath as described. While it is preferable to prepare the glassware on the day preceding the tests, the tubes are fit for use any time within a period of several days after preparation.

Influence of Temperature on the Velocity of the Complement Fixation. It has become customary to carry out immunity reactions *in vitro* at the temperature of 37° C., because most of the reactions between specific antibodies and antigens take place only at 37° C. or near that point. The reactions of bacteriolysis, cytolysis, hemolysis, agglutination, precipitation, phagocytosis, and opsonization, manifest their maximum activities at 37° C. Certain biologic reactions, however, do not necessarily follow this general rule. For example, hemolysis produced by saponin, bile salts, cobra lecithid, or sodium oleate is complete within a very short time whether at 4° or 37° C. The velocity of the reaction in these instances is such that time and temperature play but a slight part.

The mechanism of the lipotropic complement fixation of syphilitic serum or spinal fluid is not understood, but it is certain that the lipoids are an important factor. The question in regard to the velocity of this reaction has not received as much attention as it deserves. The prevailing idea is that it is one of the immunity reactions, which manifest their maximum activity at 37° C. Whether or not the reaction can take place at lower temperature has not been carefully studied until recently.

Using the acetone-insoluble fraction of tissue lipoids as antigen Noguchi⁹ found that examination of syphilitic serum or cerebrospinal fluid can be made at any temperature between 23° and 37° C. The velocity of the fixation reaction, including the fixation of complement and subsequent hemolysis, is greater at a higher temperature; the optimum point was found to be 37° C. The maximum reaction is also reached, however, when the mixture of lipoids, syphilitic serum, and complement is allowed to stand for a long enough period at a lower temperature with the minimum thermal point near 23° C. For the optimum temperature (37° C.) an incubation of 30 minutes is sufficient, whereas for the minimum temperature (23° C.) two hours are necessary. At the temperature of 30° C. the reaction proceeds with moderate velocity and is complete within sixty minutes.

Guinea-pig complement gave a sharper reaction with the sera which contained less than one unit of the fixing substance. Fixation is complete, however, at any of the three temperatures within twenty minutes when there are more than two units present. A serum containing one unit of fixing substance will complete reaction within thirty minutes at 37° C., sixty minutes at 30° C., and two hours at 23° C., irrespective of whether human or guinea-pig complement is used.

For many reasons, a properly adjusted thermostat for 37° C. is recommended for conducting the serum diagnosis of syphilis when possible, but it should not be overlooked that at a temperature near 30° C. an entirely reliable result can be obtained without a special incubator. Even at a temperature as low as 23° C. the

(9) Jour. Exper. Med., September, 1918.

test can be carried out if sufficient length of time is allowed.

Binding of Complement at Low Temperatures. In a previous report by E. H. Ruediger,¹ it was shown that complement was bound better at a temperature of about 10° C. than at 37° C. It was shown also that complement binding progressed slowly so that many hours are required for its completion. At that time the optimum temperature for complement binding and the time necessary for its completion had not been determined and dealt with at this time.

The author now finds that incubation at 1° C. gave stronger positive results than did incubation at 2° C., 3° C., 4° C., 5° C., 6° C., 7° C., 8° C., 9° C., 10° C., or 37° C., while the results obtained at 0.5° C. were identical with those obtained at 1° C.

Incubation for twenty-four hours at 1° C. gave stronger positive results than incubation at 1° C., for fifteen hours; incubation for fifteen hours at 1° C. gave stronger positive results than did incubation for ten hours at 1° C.; incubation for ten hours at 1° C. gave stronger positive results than did incubation for five hours at 1° C., and incubation for five hours at 1° C., gave stronger positive results than did incubation for one hour at 1° C.

Incubation for ten hours at 1° C., gave uniformly good results, whilst with one lot of complement 15-hour incubation at 1° C., and 24-hour incubation at 1° C., gave poor results. At the present time 10-hour incubation at 1° C., is the longest incubation time which has met all requirements.

Twenty-four serums from healthy persons gave negative results under 10-hour incubation at 1° C., and under 15-hour incubation at 1° C.

Alcoholic extract of beef heart gave much stronger positive results than did acetone-insoluble antigen of beef heart. The alcoholic extract gave the strong positive results at 1° C., while the acetone insoluble antigen gave stronger positive results at 37° C. than at 1° C.

At 1° C., alcoholic extract of beef heart gave results

(1) Jour. Inf. Dis. 1918, p. 173.

that were identical with the results given by alcoholic extract of human heart at 1° C.

Acetone-insoluble antigen of beef heart gave much weaker positive results than did alcoholic extract of human heart.

Warming the serum-complement-antigen mixture before the sensitized blood corpuscles were added gave the same results as when the sensitized blood corpuscles were added to the cold serum-complement-antigen mixture. Warming the serum-complement-antigen mixture before the sensitized blood corpuscles are added is a decided advantage because hemolysis is much more rapid and agglutination of the corpuscles is much less.

Fixation of Complement at Icebox Temperature. In 1916, Smith and MacNeal¹ showed the increased sensibility of the Bordet-Wassermann test when the first incubation is carried out at 8° C. instead of at 37° . These authors used only the simple alcoholic antigen in

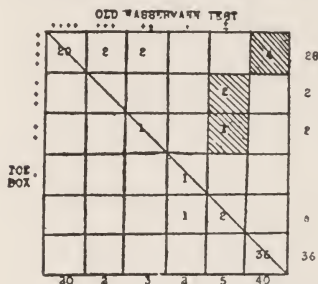


Fig. 3. Primary syphilis: Wassermann reaction in seventy-two cases on admission; shaded figures (seven cases) would have passed as negative with old Wassermann test.

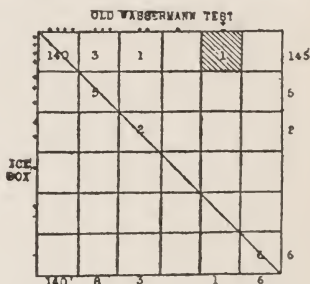


Fig. 4. Secondary syphilis: Wassermann reaction in 158 cases on admission; shaded figure (one case) would have passed as negative with old Wassermann test.

the icebox incubation, but even so this method was more sensitive than the cholesterolized antigen at 37° C.

Wile and Hasley² have made a careful study of the comparative sensitiveness of the icebox and body temperature incubation methods in 459 selected cases. The same cholesterolized antigen was used in all tests.

(1) Practical Medicine Series, 1917, Vol. IX., p. 174.
 (2) Jour. Amer. Med. Ass'n., May 24, 1919.

Of the cases which were observed over the period of eighteen months, there were available for close scrutiny only thirty-nine in which the authors were satisfied that intensive therapy was carried out, and in which repeated tests were made. The treatment instituted in all these cases was in the form of courses of arsphenamin or neoarsphenamin, and no patient received less than six injections and most of the cases under discussion received two such courses, together with intensive mercurialization over a greater portion of the period of observation with inunctions or injections (Figs. 3 to 11).

From a study of Figures 7 and 8 it will be noted that

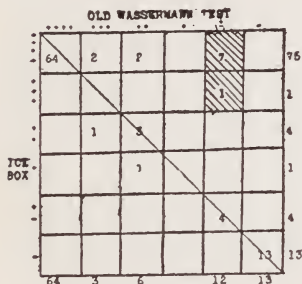


Fig. 5. Tertiary syphilis: Wassermann reaction in ninety-eight cases on admission; shaded figures (eight cases) would have passed as negative with old Wassermann test.

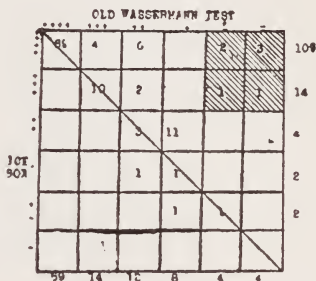


Fig. 6. Latent syphilis: Wassermann reaction in 131 cases on admission; shaded figures (seven cases) would have passed as negative with old Wassermann test.

of thirteen cases of secondary syphilis on admission, in only one case is any difference to be noted in the reaction of the serum in both tests. After treatment, however, it will be seen (Fig. 8) that eight cases became negative or doubtful and remained so with the old test while still giving a strongly positive reaction to the icebox test.

In the group of tertiary syphilis cases studied over this period in which treatment had been instituted and the patients had been under careful and frequent observation, there were sixteen cases. Of these (Fig. 9), on admission four, by reason of negative tests with the old Wassermann, might well have escaped recognition. These four gave strongly positive reactions in the icebox. After

treatment, however (Fig. 10), a great degree of divergence occurs in these cases. Nine became negative or

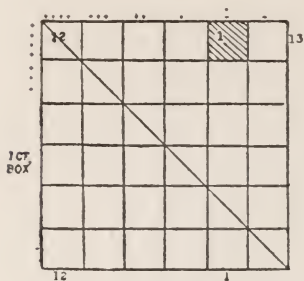


Fig. 7. Thirteen treated cases of secondary syphilis on admission: Shaded figure (one case) would have been considered doubtful on admission on basis of old Wassermann test.

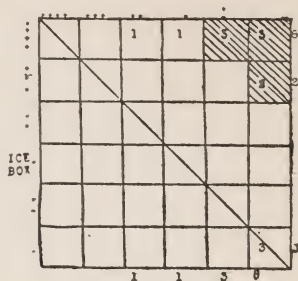


Fig. 8. Thirteen treated cases of secondary syphilis after treatment: Shaded figures (eight cases) would have been considered as cured on basis of old Wassermann test.

doubtful and would thus be considered as progressing toward serologic cure and by some perhaps cured, whereas all of these still gave strongly positive reactions

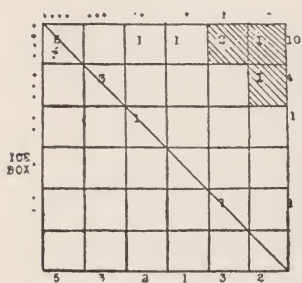


Fig. 9. Sixteen treated cases of tertiary syphilis on admission: Shaded figures (four cases) would have been considered doubtful on admission on basis of old Wassermann test.

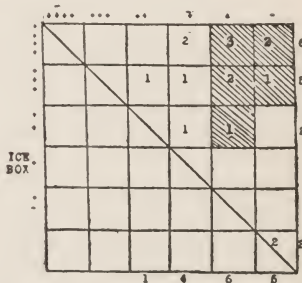


Fig. 10. Sixteen cases of tertiary syphilis after treatment: Shaded figures (nine cases) would be considered as cured on basis of old Wassermann test.

in the icebox test. A further study of the chart reveals on the part of the five other cases a gradual approach toward the negative phase with the old test, with little

or no difference in the intensity of the reaction with the icebox. Two cases became uniformly negative with both tests. Of the group of latent cases, only ten were available as having been assiduously treated and frequently tested over the period of observation. Of these on admission (Fig. 11) a uniform finding is noted by both tests in all cases. After treatment, however, five cases became negative or doubtful with the old test and

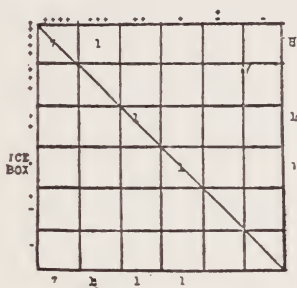


Fig. 11. Ten treated cases of latent syphilis on admission: uniform findings in both tests.

thus might have been considered as cured or approaching serologic cure, whereas the icebox test revealed them as still strongly positive. This illustrates the gradual diminution of sensitiveness in the old test in the remaining cases as against practically constant, intensely positive reactions as shown by the icebox test.

To sum up therefore, it would appear that in a total of thirty-nine cases, treated over the period of eighteen months, only six cases became serologically negative with the icebox test, as against twenty-two, or more than 50 per cent. which became apparently negative with the old test.

Frozen Complement in the Wassermann Reaction. Without giving any details, Moledzky³ says that frozen complement retains its strength indefinitely. As complement usually deteriorates within three days it is the most expensive ingredient in the Wassermann reaction,

(3) Practical Medicine Series, 1918, Vol. VII, p. 210.

and as the time for standardization is short a method by which complement can be preserved is very desirable. Other methods have been found unsatisfactory, frozen complement was studied by E. H. Ruediger⁴ who found that frozen guinea-pig complement one week old, whether composed of the mixed serums of three guinea-pigs or of the serum from one guinea-pig usually gave a little stronger positive result with the Wassermann reaction than did the same complement while fresh. At the age of two weeks the frozen complement gave results that were nearly identical with the results obtained with the fresh complements. After two weeks the frozen complement gradually lost strength, apparently more rapidly in mild weather than in very cold weather.

Efficiency of Different Antigens. A comparative study by Browning and Kennaway⁴ of results obtained by liver-lecithin-cholesterol antigen and heart-cholesterol antigen shows that the former gives about 6 per cent. more positive reactions than does the latter. The following is a tabulation of the results:

Table Showing Results with the Two Antigens.

Heart-cholesterol.	Liver-lecithin-cholesterol.	Number of sera.	Result.
+	+	125	Agreement in 83 per cent.
—	—	165	
?	?	9	
+	— or ?	15 = 4.2%	Difference of result in 17 per cent.
?	—	1 = 0.28%	
— or ?	+	21 = 5.8%	
—	?	24 = 6.6%	
Total....		360	

A further point which it is of importance to bear in mind in connection with further work on antigens, is that not merely may one antigen differ from another as regards optimum concentration, but also that the amount of serum necessary to elicit the maximum complement fixation may vary. Thus, with the heart-cholesterol antigen reduction in the amount of serum, recommended by McIntosh and Fildes, leads to a striking reduction in

(4) *Lancet*, Nov. 30, 1918.

(4) *Jour. Inf. Dis.*, September, 1919.

the amount of complement fixation, whereas a similar reduction does not lead to this effect when liver lecithin-cholesterol is used as antigen.

These results have led to the adoption of the following procedure in conducting routine Wassermann tests:

For each serum two series of three tubes each are set up: (a) containing liver-lecithin-cholesterol (1/8 turbid emulsion) 0.3 c.cm. plus 0.125 c.cm. patient's heated serum; and (b) heart extract plus cholesterol (1/30 rapidly mixed emulsion) 0.5 c.cm. plus 0.05 patient's heated serum, along with increasing amounts of complement in each series. Thus the procedure is practically the same as that described in the Medical Research Committee's Report except that the heart extract plus cholesterol is substituted for the emulsion of lecithin alone.

It is strongly urged that the uncertainty which at present exists with regard to the significance of the behaviour of certain sera can be best cleared up by a collective investigation concentrated on such cases, and that three classes of material are required: (1) cases of syphilis known to have reacted positively, in which the reaction is becoming extinguished as the result of treatment; (2) untreated cases of congenital syphilis in which other children of the family or the mother are definitely positive; and (3) cases in which, although there is no clinical suspicion of syphilis, doubtful or positive reactions have been obtained. An extensive selection of negative controls is also highly desirable; these might best be obtained voluntarily from among laboratory workers.

The Influence of Antigen Dilution on the Wassermann Reaction. In a previous report it was shown that higher dilutions of antigens gave stronger positive results in the Wassermann reaction than did lower dilutions of the same antigen. The results obtained in a more detailed study on the influence of antigen turbidity and antigen dilution are reported by E. H. Ruediger.⁵

He found that the turbidity of the antigen solution and the the dilution of the antigen solution greatly influenced the results obtained with the Bordet-Wassermann reaction with serums from syphilitic persons. For each

antigen there seems to be an optimum turbidity and an optimum dilution. Antigen diluted too slowly or too rapidly lost in antigenic value.

The optimum dose of antigen would be the proper dose to use in the Wassermann reaction. The optimum dilution of antigen may be somewhat higher than is commonly used; alcoholic extract of human heart gave the strongest positive results in a dilution of 1/50 and alcoholic extract of beef heart and of rabbit heart gave the strongest positive results in dilutions of 1/100.

When the antigen was diluted too slowly the optimum dilution of that particular solution was low, and when the antigen was diluted too rapidly the optimum dilution of that particular solution was high; but neither was equal in antigenic value to the optimum dilution of the optimum turbidity. With serums from non-syphilitic persons the results were uniformly negative.

Human Complement in Serum Diagnosis. The growing scarcity of guinea-pig serum, and the difficulties of obtaining sheep corpuscles under war conditions, have emphasized the importance of so modifying the Bordet-Wassermann reaction that these difficulties may be overcome. The particular value of the new Noguchi, and of the Hecht-Gradwohl reactions is dependent largely on their simplicity and the utilization of human complement.

Kolmer⁶ has made extensive, and carefully controlled tests of these methods and has reported the results of his work. The author finds that both tests conducted with active sera are very delicate and serve to detect syphilis antibody under conditions in which the Bordet-Wassermann reaction may be negative even with cholesterolized-antigen. For this reason, he regards a negative Noguchi and Hecht-Gradwohl reaction better evidence of the absence or cure of syphilis than a negative Bordet-Wassermann.

Of greater importance is the question of pseudo or falsely positive reactions which may result when active sera are used, and particularly under the conditions of these tests when the patients' own serum is used as complement. The Hecht-Gradwohl test when conducted

(6) Amer. Jour. Syph., October, 1918.

with an acceptable antigen of acetone insoluble lipoids titrated with active human serum is reliable in this respect. With the new Noguchi test using 0.1 c.c. of active serum there occurred from 1 to 4 per cent. of pseudo-reactions which are ascribed more to slight deterioration of complement or weak hemolysin than to proteotropic reactions due to defective antigen, inasmuch as a repetition of the tests with fresh sera usually yielded negative reactions. The Noguchi homohemolytic tests conducted with 0.2 c.c. serum yielded no falsely positive reactions but gave too many falsely negative reactions owing to the excess of complement present. The results with Noguchi's new test which makes use of inactivated serum and cerebrospinal fluid with human complement were decidedly unsatisfactory on account of the occurrence of a high percentage of anticomplementary or indefinite reactions.

The necessity of using perfectly fresh sera in both the Noguchi and the Hecht-Gradwohl tests for the best results is an objection or not depending on circumstances, inasmuch specimens must be collected on certain days or the tests must be conducted daily.

In both tests, the antigen of acetone-insoluble lipoids is most reliable particularly from the standpoint of pseudo or falsely positive reactions. The antigen for both tests should be titrated at frequent intervals with human serum instead of with guinea-pig complement. In the Noguchi test it is important to use as powerful antihuman hemolysin as possible in order to avoid the disturbing factor of hemagglutination, and the difficulty of preparing sufficiently active hemolysin may constitute a drawback to the test. For this reason the author prefers the Hecht-Gradwohl test and believes it to be technique of choice when using human complement, if sheep cells be available.

The technique of both the Noguchi homohemolytic and the Hecht-Gradwohl tests has been successfully applied in the diagnosis of gonococcus infections in a small series of cases.

The final acceptance of either of these tests as substitutes for the Bordet-Wassermann reaction will depend largely upon the experience of the individual serologist.

Those experienced in the use of the Bordet-Wassermann test are likely to accept them more as controls than as routine tests. The author is of the opinion that either may be used as routine tests provided proper antigen be available, and sufficiently active hemolysin for the Noguchi tests, but that positive reactions should be repeated and then checked up with the Bordet-Wassermann. The latter should be available for testing the 8 per cent. of sera which contain too little complement or hemolysin or both for the conduct of either test using the patient's serum for complement.

Increasing the Titer of Antisheep Amboceptor by Chemical Fractionation. Variation in the potency of antisheep amboceptor occurs within wide limits. The necessity of having a high titer serum is well recognized.

Kosakai⁷ gives a method for the isolation, purification and concentration of amboceptor. To a 1/100 dilution of inactivated antisheep amboceptor in normal saline, add enough washed sheep's red cells to absorb the the amboceptor from the red cell. Then centrifugalize fluid. Suspend the amboceptor red cell combination of 10 per cent. saccharose solution and shake to separate the amboceptor from the red cell. Then centrifugalize to remove the cells. Shake with ether to remove traces of hemoglobin. Dialyze the saccharose-amboceptor mixture to remove the sugar. Finally, concentrate the purified amboceptor in an exsiccator. This process is so complicated that it would be difficult to prepare large amounts of amboceptor.

A simpler method has been devised by Gilbert and Van Saun.⁸ The pooled sera of a number of rabbits, having titers ranging from 1/300 to 1/500, was titrated and found to give complete hemolysis with 0.08 c.c. in a dilution of 1/300. The globulin fraction was then separated by means of precipitation with ammonium sulphate. This fraction gave complete hemolysis with 0.05 c.c. of a 1/500 dilution. The albumin fraction gave no hemolysis even with 0.1 c.c. of the undiluted material.

Further separation of the globulin fraction into pseudo-globulin and euglobulin gave complete hemolysis with 0.08 c.c. of a 1/500 dilution of the pseudo-globulin

(7) Jour. Immunology, 1918, No. 3.

(8) Amer. Jour. Syph., October, 1918.

and complete hemolysis with from 0.02 c.c. to 0.01 c.c. of the undiluted euglobulin, thus showing that although most of the immune body is apparently in the pseudoglobulin fraction enough is contained in the euglobulin fraction to make a union of the two desirable, and therefore to render it unnecessary to separate the two globulin fractions. If the globulin has become too dilute while dialyzing, the excess of water may be easily removed by the Kober method of pervaporation. The dialyzing bag may be hung in front of an electric fan until the globulin fraction is sufficiently concentrated. From these results it seems possible to increase the potency of low antisheep amboceptor by removing the inert albumin fraction.

The New System of Noguchi and That of McIntosh and Fildes. A comparative study by Lewis and Newcomer⁹ shows that the Wassermann reaction carried out according to the method of McIntosh and Fildes, with cholesterolized antigen and with certain allowances for the presence of native antisheep amboceptor, leads to about the same result as when it is done according to the recent proposal of Noguchi, with the native human complement and acetone-insoluble lipoids as antigen. The differences are such as to suggest that from the point of view of diagnosis the Noguchi method is the more conservative but that there is definite advantage in using two methods as distinct in origin of materials as these, partly for the purpose of control and partly in the hope of acquiring new information of importance. As a measure of control of treatment, the cholesterol antigen appears to be the more valuable. The Wassermann reaction alone, by whatever method it may be done, can only be used in the diagnosis of syphilis in conjunction with presumption based on other grounds. That it fails to appear in a considerable percentage of syphilitics is well known. That the reaction is positive in other conditions is not so generally recognized. Fresh instances of this in certain febrile cases are here recorded.

Clinical Value of the Bordet-Wassermann Reaction. Chadzinski in a recent meeting of *la Société Française de Dermatologie* stated that the Bordet-Wassermann reaction is more dangerous than useful, not only for pur-

(9) Jour. Exper. Med., April, 1919.

poses of the diagnosis but for treatment as well. His experience in the army had shown that the formula of a plus or minus reaction had tended to replace clinical judgment, and that a great many most flagrant errors had been committed because the clinician had been led astray by defective laboratory technique in conducting the reaction. Revaut, Milian and Leredde took the opposite view. Carle of Lyon² has given his experience in attempting to carry out the Bordet-Wassermann reaction in the French army under the most adverse circumstances. In the early days of the war he was obliged to work with improvised apparatus, and the necessity of the laboratory being ambulatory caused a great deal of confusion. Later, when the venereal centers were established, opportunities for the organization of proper laboratory facilities occurred. Under the stress of war it was not surprising that about 67 per cent. of his results had been what he terms "acrobatic." Physicians soon acquired the habit of sending patients for Bordet-Wassermann reactions rather than taking the trouble of investigating their cases from a clinical standpoint. The result was that their judgment was erroneous and a great deal of harm was done to a large number of patients. In 1917, the author became thoroughly established in a laboratory having proper facilities for carrying out the tests, and he made a careful study of the value of the test as carried out in the army. He found that in the primary period 80 per cent. of the cases gave strongly positive results when the reaction was carried out fifty days after the exposure had taken place. During the secondary period 93 per cent. of the cases were positive. In the tertiary period 86 per cent. of the cases gave positive reactions and two cases with typical skin lesions were negative. Both of these cases, however, became positive after a short period of treatment. In the non-specific cases, 90 per cent. of the reactions were negative, and this 10 per cent. of positive reactions in supposedly negative cases he explains on the basis of latent syphilis co-existing with other conditions and going unrecognized.

(2) Bull. Soc. franc. de dermat. et de syph., 1919, Nos. 5 and 6.

Reliability of The Bordet-Wassermann Test. So much criticism has been made of the reliability of this test that it is comforting to those of us who have faith in it, when properly controlled, to read a report such as is made by White, McWhirter and Barber.³

The cases forming the basis of this paper were all carefully studied clinically and serologically and so far as possible the cases were followed up for some time after the tests were made.

1. *Cases Clinically Syphilitic:* (a) **Primary Syphilitic Sores:** Out of a series of 117 primary sore cases ninety-nine gave strong positive reactions, eight gave partial positive results, and there were ten negative readings, explained by test being performed early in the disease. With spirochetes demonstrated in the sore an early test with a negative result may confirm the clinical opinion that the case is one of reinfection in a patient who had had syphilis before and who had been cured, and that there it is not a relapse.

(b) **Secondary Syphilitic Cases and Relapsed Cases with Secondary Lesions:** In a series of 177 such cases, 174 gave strong positive reactions, two gave partial positives, and one was weakly positive. The three partial results were relapsed cases treated formerly with arsphenamin; they were not tested again after provocative injections.

(c) **Tertiary Cases:** Of 125 tertiary cases of all varieties 117 gave strong positive reactions, five gave partially positive, and two cases of leukoplakia, apparently syphilitic in origin, were negative; it is not impossible for cases with such healed lesions to give negative reaction. There remained one case of what appeared to be tertiary ulceration of the throat which gave a negative reaction and also negative reactions at two other hospitals; the condition did not clear up very quickly under antisypilitic treatment, but it healed and the case was regarded as one of gummatous ulceration with a negative Wassermann.

(d) **After-Treatment Results:** In a series of cases classified as primary syphilis, the result after the end of a minimal course (consisting of seven intravenous

(3) Lancet, March 29, 1919.

injections of arsphenamin and seven mercury injections) was negative in 83.5 per cent. The total quantity of arsphenamin was 2.8 g.

In a series of cases of secondary syphilis, the percentage of negative results after a similar course was 58.1. The cases classified as secondary are those with condylomata, mucous patches, or a rash, so some of those under the heading of primary may be very late ones. The Wassermann test is taken quite soon after the last injection and may be more positive than it will be a few weeks later.

2. *Cases Which Clinically Were Not Syphilitic:* (a) Soft Sore Cases: Cases clinically soft chancre were not finally diagnosed as such until the patient had been under observation for a month from appearance of the sore and then gave a negative Wassermann reaction. Though not practicable under war conditions, such cases should be under observation for not less than two months, and have the test repeated at the end of the second month.

There are 547 of these cases divided into two series. The first of 337 cases showed twelve positive Wassermann results; the cases were not specifically studied at the time for this investigation, but the clinical cards for about half of these twelve were traced and showed that the cases were accepted for antisyphilitic treatment.

The second series of 209 cases was carefully studied to test the reliability of the Wassermann reaction; each unexpected result was investigated at the time. The pathologists frequently obtained a provisional diagnosis of soft sore in the laboratory, which was somewhat out of date or made before the patient was admitted, and by no means the clinical opinion at the time of the test; but the reading was given by them without any indication that the case might be syphilitic. Twenty-one such cases gave a positive result; and were carefully investigated. Four were proved syphilitic by finding spirochetes; three other cases showed evidence of syphilis as follows: One gave a definite history, with knowledge that his blood had been positive before, the second showed a tertiary skin lesion, and the third the scar typical of a primary granulating syphilitic sore on the penis. Of the remaining fourteen cases, seven were sent by the clinician as

venereal sores for diagnosis, very suggestive of primary syphilis, and after the result were accepted as such. Those cases tested after treatment gave a negative result, suggesting that a recent syphilitic infection had been cured. The seven other cases were typical soft sore cases, with no evidence of syphilis, and there is no clinical explanation of the result. They were tested more than once, and those tested after treatment gave a positive result as would be expected of a latent syphilitic, in contrast to the cases above, grouped as primary sores for diagnosis. There is no explanation, in the way of proof, but seven out of 209 men with venereal sores would not seem a very high proportion of latent syphilis.

This series of 547 soft sore cases, which represents the whole batch for six months, is the most valuable one by way of normal control. A critic, the most prejudiced against the reliability of the test, could only object to about 3 per cent. of positive results. Considering that the men all admittedly had venereal sores of some sort, it would not appear to show undue bias in favor of the test to claim so small a percentage as latent syphilitics.

(b) Cases from the Skin Wards: Eighty-nine cases were sent in six months from these wards; in the laboratory when the reading is taken the presumption was that the case was not syphilitic. Of the eighty-nine cases seventy-eight were negative, being all varieties of skin lesions not syphilitic. The eleven remaining were as follows: four strongly positive were tertiary skin lesions, quite obvious, being tested before treatment; four more strong positives were readily explained; a case of psoriasis gave a history of syphilis in 1917; a case of vitiligo the same; a case of impetigo showed tuberosities on the tibia and admitted syphilis; and another case of impetigo showed the scar of a primary granulating sore on the penis. One case of psoriasis gave a doubtful reading with a bad serum control, and a case of psoriasis and another of vitiligo gave strong positives which could not be explained. So that finally, if the result be accepted as a sign of syphilis in these two cases it only means two latent syphilitics in eighty-nine soldiers.

Of special skin cases one of the most interesting is the following: A case of papulo-squamous eruption,

serpiginous and circinate in outline, on both arms, very suggestive of a tertiary syphilide, gave a negative reaction three times, the later ones after arsphenamin injection; the condition was proved tuberculous by microscopic examination of a section of the lesion.

Positive Bordet-Wassermann Reaction in Tuberculids. The question of the specificity of the Bordet-Wassermann reaction has been the subject of much discussion, and is still an open question. It has long been thought that in some cases of tuberculosis the Bordet-Wassermann may give a false positive. Ravaut studied intensively the question of positive Bordet-Wassermann reactions in cases of tuberculids and found in three cases of the papulonecrotic tuberculides, one of which was associated with angiolupoid and another with lupus erythematosus in which the reaction was positive. He also found a positive reaction in a case of sarcoid and in a case of angiolupoid. In all of these five cases he stated himself that syphilis was absent but arsphenamin gave excellent results in the treatment and in some cases led to complete cure. Inasmuch as this occurred, the presence of syphilis could not be definitely excluded. Schaumann⁴ of Stockholm studied two cases, one of which was lupus erythematosus associated with papulonecrotic and nodular tuberculids, and the other a case of papulo and nodular tuberculids. In both the Bordet-Wassermann reaction was strongly positive but in neither could the author find any evidence of syphilis. The Bordet-Wassermann tests were carefully controlled and the author is satisfied of the accuracy of the results. In the first case he attempted to obtain a negative reaction by the injection of mercury but was unable to bring this about.

Bordet-Wassermann Reaction and the Chancre. Owing to the fact that he has been unable to find *Spirochaeta pallida* in clinically typical cases J. P. Walker⁵ urges early resort to the Bordet-Wassermann reaction as an aid in diagnosis.

The figures in all these tables were collected from a consecutive series of 500 venereal cases referred for diagnosis, and on whom a Bordet-Wassermann reaction

(4) Ann. de dermat. et de syph., September, 1918.

(5) Practitioner, May, 1919.

was carried out, at the Central Venereal Hospital, Lichfield, 1915. The serum reaction was either the original one of Wassermann or the modification of Stern. The percentages are to the nearest whole number.

Length of Time Since Patient Noticed Any Venereal Sore to Performance of Wassermann.

Weeks.	Posi- tive.	Doubt- ful.	Nega- tive.	Total.	Per cent. Posi- tive.	Weeks.
0-1	3	7	13	23	13	0-1
1-2	11	17	15	43	24	1-2
2-3	43	25	13	81	53	2-3
3-4	41	10	21	72	57	3-4
4-5	26	11	8	45	58	4-5
5-6	23	9	12	44	52	5-6
6-7	12	2	3	17	70	6-7
7-8	19	4	4	27	70	7-8
8-12	28	3	10	41	68	8-12
12-16	15	5	3	23	65	12-14
16-24	9	1	4	14	64	16-26
24 onwards	25	4	3	32	78	24 onwards

Length of Time from Contagion (presumed) to Appearance of any Venereal Sore.

Weeks.	Posi- tive.	Doubt- ful.	Nega- tive.	Total.	Per cent. Posi- tive.	Weeks.
0-1	71	30	53	154	46	0-1
1-2	42	21	16	79	53	1-2
2-3	27	10	10	47	57	2-3
3-4	26	13	10	49	53	3-4
4-5	11	3	2	16	60	4-5
5-6	16	3	2	21	76	5-6
6-8	8	2	2	14	67	6-8
8-12	9	0	3	12	75	8-12
12 onwards	6	3	0	9	67	12 onwards

Length of Time from Contagion (presumed) to Performance of Wassermann.

Weeks.	Posi- tive.	Doubt- ful.	Nega- tive.	Total.	Per cent. Posi- tive.	Weeks.
0-3	7	14	23	44	16	0-3
3-4	24	16	20	60	40	3-4
4-5	24	17	20	61	39	4-5
5-6	23	14	15	52	44	5-6
6-7	17	8	9	34	50	6-7
7-8	31	8	10	49	63	7-8
8-12	49	13	18	80	61	8-12
12-16	11	1	2	14	78	12-16
16 onwards	28	6	7	41	68	16 onwards

From a survey of his statistics, the author concludes that:

1. A Wassermann reaction is positive, in a considerable percentage of cases much sooner after the detection of the chancre by the patient than is generally supposed. No less than 24 per cent. gave a positive reaction in the second week.

2. Out of 154 patients who noticed the appearance of a venereal sore within eight days from presumed infection, 46 per cent. ultimately gave a positive reaction.

3. A positive Wassermann reaction may be obtained very soon after the presumed contagion; 16 per cent. within three weeks; 40 per cent. in four weeks.

4. All these cases it must be understood were venereal cases, and undoubtedly many must have had syphilis earlier in life and the examination of the serum revealed the taint.

5. In a venereal case it is never "too early for a Wassermann."

[There is something wrong with the technique, or with the operator who can not find *Spirochaeta pallida* in "clinically typical cases." The examiner either does not know how, or lacks the patience and care necessary to find the organisms. The technique of the examination is looked upon by many clinicians as being a mechanical process and therefore beneath their dignity. The result is that it is left to some novice about the laboratory who has neither the training in the technique, nor the judg-

ment required to distinguish between *Spirochaeta pallida* and other spirilla.

The danger of getting a false positive Bordet-Wassermann reaction in a non-syphilitic lesion of the penis is an ever-present danger, as has been repeatedly pointed out in these volumes. In his fourth conclusion, the author says that "all were venereal cases, and undoubtedly many must have had syphilis earlier in life and the examination of serum revealed the taint." This is perfectly true but it has failed to help in the diagnosis of the chancre. In such a case, the positive reaction proves rather conclusively that the lesion is not a chancre (assuming of course that the reaction had been carried out by a reliable worker), but the inexperienced clinician is almost certain to be convinced thereby that it is a chancre and he will treat the patient accordingly.

In our experience the average practitioner relies entirely too much on the value of the Bordet-Wassermann in lesions of the genitalia. Many chancres are missed because the reaction is negative, and many non-syphilitic lesions are considered as chancres because of a false-positive or because the patient is syphilitic and has a pre-existing positive.—M.]

The Incidence of Syphilis as Shown by the Bordet-Wassermann Test. Two thousand nine hundred and twenty-five hospital and dispensary patients were subjected to a routine Bordet-Wassermann test during the year 1918 by Day and McNitt. The incidence of syphilis as shown by the Bordet-Wassermann reaction was found to be lowest among the well-to-do, about twice as high among the middle class of society, represented by the pay-ward patients, and about three times as high among the lower social class, or free-ward patients. The incidence of syphilis among colored patients was about six times that among private patients.

About 15 per cent. of cases giving strongly positive reactions gave no clinical evidence of syphilis. This percentage increases with the cholesterol-positive cases, indicating that a certain number of cases giving weakly positive Wassermann reactions with the cholesterol antigen only did not have syphilis.

The percentage of clinically positive syphilis is high-

est in the strongly positive group (61 per cent.) and lowest in the +1 positive cholesterol cases (7.3 per cent.). Weak reactions with the cholesterol antigen are of value only when there is a definite clinical evidence of syphilis, in treated cases, or in cases of neurosyphilis.

Of 853 white males, 30 per cent. gave positive Wassermann reactions; of 924 females, 16 per cent. were positive. Among colored patients 48 per cent. of 200 males and 40 per cent. of 273 females gave positive Bordet-Wassermann reactions. Among seven cases of diabetes giving positive Wassermann reactions, only one did not give clinical evidence of syphilis. Of four cases of malaria giving positive Wassermann reactions it seems probably that two of the positive reactions were due to malarial infection and not to syphilis.

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